90

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 September 2003 (25.09.2003)

PCT

(10) International Publication Number
WO 03/078662 A1

(51) International Patent Classification[7]: C12Q 1/68, G01N 33/53

(21) International Application Number: PCT/US03/07713

(22) International Filing Date: 12 March 2003 (12.03.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/364,890 13 March 2002 (13.03.2002) US
60/412,049 18 September 2002 (18.09.2002) US

(71) Applicant *(for all designated States except US)*: GENOMIC HEALTH [US/US]; 301 Penobscot Drive, Redwood City, CA 94063 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BAKER, Joffre, B.** [US/US]; P.O. Box 371212, Montara, CA 94937 (US). **CRONIN, Maureen, T.** [US/US]; 771 Anderson Drive, Los Altos, CA 94024 (US). **KIEFER, Michael, C.** [US/US]; 401 Wright Court, Clayton, CA 94517 (US). **SHAK, Steve** [US/US]; 1133 Cambridge Road, Burlingame, CA 94010 (US). **WALKER, Michael, G.** [US/US]; 1475 Flamingo Way, Sunnyvale, CA 94087 (US).

(74) Agent: **DREGER, Ginger, R.**; Heller Ehrman White & McAuliffe, 275 Middlefield Road, Menlo Park, CA 94025-3506 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/078662 A1

(54) Title: GENE EXPRESSION PROFILING IN BIOPSIED TUMOR TISSUES

(57) Abstract: The invention concerns sensitive methods to measure mRNA levels in biopsied tumor tissues, including archived paraffin-embedded biopsy material. Th invention also concerns breast cancer gene sets important in the diagnosis and treatment of breast cancer, and methods for assigning the most optimal treatment options to breast cancer patient based upon knowledge derived from gene expression studies.

GENE EXPRESSION PROFILING IN BIOPSIED TUMOR TISSUES

Background of the Invention

Cross-Reference

This application claims the benefit under 35 U.S.C. 119(h) of provisional applications serial nos. 60/412,049, filed September 18, 2002 and 60/364,890, filed March 13, 2002, the entire disclosures which are herby incorporated by reference.

Field of the Invention

The present invention relates to gene expression profiling in biopsied tumor tissues. In particular, the present invention concerns sensitive methods to measure mRNA levels in biopsied tumor tissues, including archived paraffin-embedded biopsy material. In addition, the invention provides a set of genes the expression of which is important in the diagnosis and treatment of breast cancer.

Oncologists have a number of treatment options available to them, including different combinations of chemotherapeutic drugs that are characterized as "standard of care," and a number of drugs that do not carry a label claim for a particular cancer, but for which there is evidence of efficacy in that cancer. Best likelihood of good treatment outcome requires that patients be assigned to optimal available cancer treatment, and that this assignment be made as quickly as possible following diagnosis.

Currently, diagnostic tests used in clinical practice are single analyte, and therefore do not capture the potential value of knowing relationships between dozens of different markers. Moreover, diagnostic tests are frequently not quantitative, relying on immunohistochemistry. This method often yields different results in different laboratories, in part because the reagents are not standardized, and in part because the interpretations are subjective and cannot be easily quantified. RNA-based tests have not often been used because of the problem of RNA degradation over time and the fact that it is difficult to obtain fresh tissue samples from patients for analysis. Fixed paraffin-embedded tissue is more readily available and methods have been established to detect RNA in fixed tissue. However, these methods typically do not allow for the study of large numbers of genes (DNA or RNA) from small amounts of material. Thus, traditionally fixed tissue has been rarely used other than for immunohistochemistry detection of proteins.

Recently, several groups have published studies concerning the classification of various cancer types by microarray gene expression analysis (see, e.g. Golub *et al., Science* 286:531-537

(1999); Bhattacharjae *et al., Proc. Natl. Acad. Sci. USA* 98:13790-13795 (2001); Chen-Hsiang *et al., Bioinformatics* 17 (Suppl. 1):S316-S322 (2001); Ramaswamy *et al., Proc. Natl. Acad. Sci. USA* 98:15149-15154 (2001)). Certain classifications of human breast cancers based on gene expression patterns have also been reported (Martin *et al., Cancer Res.* 60:2232-2238 (2000); West *et al., Proc. Natl. Acad. Sci. USA* 98:11462-11467 (2001); Sorlie *et al., Proc. Natl. Acad. Sci. USA* 98:10869-10874 (2001); Yan *et al., Cancer Res.* 61:8375-8380 (2001)). However, these studies mostly focus on improving and refining the already established classification of various types of cancer, including breast cancer, and generally do not provide new insights into the relationships of the differentially expressed genes, and do not link the findings to treatment strategies in order to improve the clinical outcome of cancer therapy.

Although modern molecular biology and biochemistry have revealed more than 100 genes whose activities influence the behavior of tumor cells, state of their differentiation, and their sensitivity or resistance to certain therapeutic drugs, with a few exceptions, the status of these genes has not been exploited for the purpose of routinely making clinical decisions about drug treatments. One notable exception is the use of estrogen receptor (ER) protein expression in breast carcinomas to select patients to treatment with anti-estrogen drugs, such as tamoxifen. Another exceptional example is the use of ErbB2 (Her2) protein expression in breast carcinomas to select patients with the Her2 antagonist drug Herceptin® (Genentech, Inc., South San Francisco, CA).

Despite recent advances, the challenge of cancer treatment remains to target specific treatment regimens to pathogenically distinct tumor types, and ultimately personalize tumor treatment in order to maximize outcome. Hence, a need exists for tests that simultaneously provide predictive information about patient responses to the variety of treatment options. This is particularly true for breast cancer, the biology of which is poorly understood. It is clear that the classification of breast cancer into a few subgroups, such as ErbB2^{+} subgroup, and subgroups characterized by low to absent gene expression of the estrogen receptor (ER) and a few additional transcriptional factors (Perou *et al., Nature* 406:747-752 (2000)) does not reflect the cellular and molecular heterogeneity of breast cancer, and does not allow the design of treatment strategies maximizing patient response.

Summary of the Invention

The present invention provides (1) sensitive methods to measure mRNA levels in biopsied tumor tissue, (2) a set of approximately 190 genes, the expression of which is important in the diagnosis of breast cancer, and (3) the significance of abnormally low or high expression

for the genes identified and included in the gene set, through activation or disruption of biochemical regulatory pathways that influence patient response to particular drugs used or potentially useful in the treatment of breast cancer. These results permit assessment of genomic evidence of the efficacy of more than a dozen relevant drugs.

The present invention accommodates the use of archived paraffin-embedded biopsy material for assay of all markers in the set, and therefore is compatible with the most widely available type of biopsy material. The invention presents an efficient method for extraction of RNA from wax-embedded, fixed tissues, which reduces cost of mass production process for acquisition of this information without sacrificing quality of the analysis. In addition, the invention describes a novel highly effective method for amplifying mRNA copy number, which permits increased assay sensitivity and the ability to monitor expression of large numbers of different genes given the limited amounts of biopsy material. The invention also captures the predictive significance of relationships between expressions of certain markers in the breast cancer marker set. Finally, for each member of the gene set, the invention specifies the oligonucleotide sequences to be used in the test.

In one aspect, the invention concerns a method for predicting clinical outcome for a patient diagnosed with cancer, comprising

determining the expression level of one or more genes, or their expression products, selected from the group consisting of p53BP2, cathepsin B, cathepsin L, Ki67/MiB1, and thymidine kinase in a cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference cancer tissue set,

wherein a poor outcome is predicted if:

(a) the expression level of p53BP2 is in the lower 10^{th} percentile; or

(b) the expression level of either cathepsin B or cathepsin L is in the upper 10^{th} percentile; or

(c) the expression level of any either Ki67/MiB1 or thymidine kinase is in the upper 10^{th} percentile.

Poor clinical outcome can be measured, for example, in terms of shortened survival or increased risk of cancer recurrence, e.g. following surgical removal of the cancer.

In another embodiment, the inventor concerns a method of predicting the likelihood of the recurrence of cancer, following treatment, in a cancer patient, comprising determining the expression level of p27, or its expression product, in a cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference

cancer tissue set, wherein an expression level in the upper 10th percentile indicates decreased risk of recurrence following treatment.

In another aspect, the invention concerns a method for classifying cancer comprising, determining the expression level of two or more genes selected from the group consisting of Bcl2, hepatocyte nuclear factor 3, ER, ErbB2, and Grb7, or their expression products, in a cancer tissue, normalized against a control gene or genes, and compared to the amount found in a reference cancer tissue set, wherein (i) tumors expressing at least one of Bcl2, hepatocyte nuclear factor 3, and ER, or their expression products, above the mean expression level in the reference tissue set are classified as having a good prognosis for disease free and overall patient survival following treatment; and (ii) tumors expressing elevated levels of ErbB2 and Grb7, or their expression products, at levels ten-fold or more above the mean expression level in the reference tissue set are classified as having poor prognosis of disease free and overall patient survival following treatment.

All types of cancer are included, such as, for example, breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer. The foregoing methods are particularly suitable for prognosis/classification of breast cancer.

In all previous aspects, in a specific embodiment, the expression level is determined using RNA obtained from a formalin-fixed, paraffin-embedded tissue sample. While all techniques of gene expression profiling, as well as proteomics techniques, are suitable for use in performing the foregoing aspects of the invention, the gene expression levels are often determined by reverse transcription polymerase chain reaction (RT-PCR).

If the source of the tissue is a formalin-fixed, paraffin embedded tissue sample, the RNA is often fragmented.

The expression data can be further subjected to multivariate analysis, for example using the Cox Proportional Hazards model.

In a further aspect, the invention concerns a method for the preparation of nucleic acid from a fixed, wax-embedded tissue specimen, comprising:

(a) incubating a section of the fixed, wax-embedded tissue specimen at a temperature of about 56 °C to 70 °C in a lysis buffer, in the presence of a protease, without prior dewaxing, to form a lysis solution;

(b) cooling the lysis solution to a temperature where the wax solidifies; and

(c) isolating the nucleic acid from the lysis solution.

The lysis buffer may comprise urea, such as 4M urea.

In a particular embodiment, incubation in step (a) of the foregoing method is performed at about 65°C.

In another particular embodiment, the protease used in the foregoing method is proteinase K.

In another embodiment, the cooling in step (b) is performed at room temperature.

In a further embodiment, the nucleic acid is isolated after protein removal with 2.5 M NH_4OAc.

The nucleic acid can, for example, be total nucleic acid present in the fixed, wax-embedded tissue specimen.

In yet another embodiment, the total nucleic acid is isolated by precipitation from the lysis solution, following protein removal, with 2.5 M NH_4OAc. The precipitation may, for example, be performed with isopropanol.

The method described above may further comprise the step of removing DNA from the total nucleic acid, for example by DNAse treatment.

The tissue specimen may, for example, be obtained from a tumor, and the RNA may be obtained from a microdissected portion of the tissue specimen enriched for tumor cells.

All types of tumor are included, such as, without limitation, breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer, in particular breast cancer..

The method described above may further comprise the step of subjecting the RNA to gene expression profiling. Thus, the gene expression profile may be completed for a set of genes comprising at least two of the genes listed in Table 1.

Although all methods of gene expression profiling are contemplated, in a particular embodiment, gene expression profiling is performed by RT-PCR which may be preceded by an amplification step.

In another aspect, the invention concerns a method for preparing fragmented RNA for gene expression analysis, comprising the steps of:

(a) mixing the RNA with at least one gene-specific, single-stranded DNA scaffold under conditions such that fragments of the RNA complementary to the DNA scaffold hybridize with the DNA scaffold;

(b) extending the hybridized RNA fragments with a DNA polymerase to form a DNA-DNA duplex; and

(c) removing the DNA scaffold from the duplex.

In a specific embodiment, in step (b) of this method, the RNA may be mixed with a mixture of single-stranded DNA templates specific for each gene of interest.

The method can further comprise the step of heat-denaturing and reannealing the duplexed DNA to the DNA scaffold, with or without additional overlapping scaffolds, and further extending the duplexed sense strand with DNA polymerase prior to removal of the scaffold in step (c).

The DNA templates may be, but do not need to be, fully complementary to the gene of interest.

In a particular embodiment, at least one of the DNA templates is complementary to a specific segment of the gene of interest.

In another embodiment, the DNA templates include sequences complementary to polymorphic variants of the same gene.

The DNA template may include one or more dUTP or rNTP sites. In this case. iin step (c) the DNA template may be removed by fragmenting the DNA template present in the DNA-DNA duplex formed in step (b) at the dUTP or rNTP sites.

In an important embodiment, the RNA is extracted from fixed, wax-embedded tissue specimens, and purified sufficiently to act as a substrate in an enzyme assay. The RNA purification may, but does not need to, include an oligo-dT based step.

In a further aspect, the invention concerns a method for amplifying RNA fragments in a sample comprising fragmented RNA representing at least one gene of interest, comprising the steps of:

(a) contacting the sample with a pool of single-stranded DNA scaffolds comprising an RNA polymerase promoter at the 5' end under conditions such that the RNA fragments complementary to the DNA scaffolds hybridize with the DNA scaffolds;

(b) extending the hybridized RNA fragments with a DNA polymerase along the DNA scaffolds to form DNA-DNA duplexes;

(c) amplifying the gene or genes of interest by *in vitro* transcription; and

(d) removing the DNA scaffolds from the duplexes.

An exemplary promoter is the T7 RNA polymerase promoter, while an exemplary DNA polymerase is DNA polymerase I.

In step (d) the DNA scaffolds may be removed, for example, by treatment with DNase I.

In a further embodiment, the pool of single-stranded DNA scaffolds comprises partial or complete gene sequences of interest, such as a library of cDNA clones.

In a specific embodiment, the sample represents a whole genome or a fraction thereof. In a preferred embodiment, the genome is the human genome.

In another aspect, the invention concerns a method of preparing a personalized genomics profile for a patient, comprising the steps of:

(a) subjecting RNA extracted from a tissue obtained from the patient to gene expression analysis;

(b) determining the expression level in such tissue of at least two genes selected from the gene set listed in Table 1, wherein the expression level is normalized against a control gene or genes, and is compared to the amount found in a cancer tissue reference set;

(c) and creating a report summarizing the data obtained by the gene expression analysis.

The tissue obtained from the patient may, but does not have to, comprise cancer cells. Just as before, the cancer can, for example, be breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, or brain cancer, breast cancer being particularly preferred.

In a particular embodiment, the RNA is obtained from a microdissected portion of breast cancer tissue enriched for cancer cells. The control gene set may, for example, comprise S-actin, and ribosomal protein LPO.

The report prepared for the use of the patient or the patient's physician, may include the identification of at least one drug potentially beneficial in the treatment of the patient.

Step (b) of the foregoing method may comprise the step of determining the expression level of a gene specifically influencing cellular sensitivity to a drug, where the gene can, for example, be selected from the group consisting of aldehyde dehydrogenase 1A1, aldehyde dehydrogenase 1A3, amphiregulin, ARG, BRK, BCRP, CD9, CD31, CD82/KAI-1, COX2, c-abl, c-kit, c-kit L, CYP1B1, CYP2C9, DHFR, dihydropyrimidine dehydrogenase, EGF, epiregulin, ER-alpha, ErbB-1, ErbB-2, ErbB-3, ErbB-4, ER-beta, farnesyl pyrophosphate synthetase, gamma-GCS (glutamyl cysteine synthetase), GATA3, geranyl geranyl pyrophosphate synthetase, Grb7, GST-alpha, GST-pi, HB-EGF, hsp 27, human chorionic gonadotropin/CGA, IGF-1, IGF-2, IGF1R, KDR, LIV1, Lung Resistance Protein/MVP, Lot1, MDR-1, microsomal epoxide hydrolase, MMP9, MRP1, MRP2, MRP3, MRP4, PAI1, PDGF-A, PDGF-B, PDGF-C, PDGF-D, PGDFR-alpha, PDGFR-beta, PLAGa (pleiomorphic adenoma 1), PREP prolyl endopeptidase, progesterone receptor, pS2/trefoil factor 1, PTEN, PTB1b, RAR-alpha, RAR-beta2, Reduced

Folate Carrier, SXR, TGF-alpha, thymidine phosphorylase, thymidine synthase, topoisomerase II-alpha, topoisomerase II-beta, VEGF, XIST, and YB-1.

In another embodiment, step (b) of the foregoing process includes determining the expression level of multidrug resistance factors, such as, for example, gamma-glutamyl-cysteine synthetase (GCS), GST-α, GST-π, MDR-1, MRP1-4, breast cancer resistance protein (BCRP), lung cancer resistance protein (MVP), SXR, or YB-1.

In another embodiment, step (b) of the foregoing process comprises determination of the expression level of eukaryotic translation initiation factor 4E (EIF4E).

In yet another embodiment, step (b) of the foregoing process comprises determination of the expression level of a DNA repair enzyme.

In a further embodiment, step (b) of the foregoing process comprises determination of the expression level of a cell cycle regulator, such as, for example, c-MYC, c-Src, Cyclin D1, Ha-Ras, mdm2. p14ARF, p21WAF1/CI, p16INK4a/p14, p23, p27, p53, PI3K, PKC-epsilon, or PKC-delta.

In a still further embodiment, step (b) of the foregoing process comprises determination of the expression level of a tumor suppressor or a related protein, such as, for example, APC or E-cadherin.

In another embodiment, step (b) of the foregoing method comprises determination of the expression level of a gene regulating apoptosis, such as, for example, p53, BC12, Bcl-x1, Bak, Bax, and related factors, NFκ-B, CIAP1, CIAP2, survivin, and related factors, p53BP1/ASPP1, or p53BP2/ASPP2.

In yet another embodiment, step (b) of the foregoing process comprises determination of the expression level of a factor that controls cell invasion or angiogenesis, such as, for example, uPA, PAI1, cathepsin B, C, and L, scatter factor (HGF), c-met, KDR, VEGF, or CD31.

In a different embodiment, step (b) of the foregoing method comprises determination of the expression level of a marker for immune or inflammatory cells or processes, such as, for example, Ig light chain λ, CD18, CD3, CD68. Fas(CD95), or Fas Ligand.

In a further embodiment, step (b) of the foregoing process comprises determination of the expression level of a cell proliferation marker, such as, for example, Ki67/MiB1, PCNA, Pin1, or thymidine kinase.

In a still further embodiment, step (b) of the foregoing process comprises determination of the expression level of a growth factor or growth factor receptor., such as, for example, IGF1, IGF2, IGFBP3, IGF1R, FGF2, CSF-1, CSF-1R/fms, SCF-1, IL6 or IL8.

In another embodiment, step (b) of the foregoing process comprises determination of the expression level of a gene marker that defines a subclass of breast cancer, where the gene marker can, for example, be GRO1 oncogene alpha, Grb7, cytokeratins 5 and 17, retinol binding protein 4, hepatocyte nuclear factor 3, integrin subunit alpha 7, or lipoprotein lipase.

In a still further aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to 5-fluorouracil (5-FU) or an analog thereof, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis;

(b) determining the expression level in the tissue of thymidylate synthase mRNA, wherein the expression level is normalized against a control gene or genes, and is compared to the amount found in a reference breast cancer tissue set; and

(c) predicting patient response based on the normalized thymidylate synthase mRNA level.

Step (d) of the foregoing method can further comprise determining the expression level of dihydropyrimidine phosphorylase.

In another embodiment, step (b) of the method can further comprise determining the expression level of thymidine phosphorylase.

In yet another embodiment, a positive response to 5-FU or an analog thereof is predicted if: (i) normalized thymidylate synthase mRNA level determined in step (b) is at or below the 15th percentile; or (ii) the sum of normalized expression levels of thymidylate synthase and dihydropyrimidine phosphorylase determined in step (b) is at or below the 25th percentile; or (iii) the sum of normalized expression levels of thymidylate synthase, dihydropyrimidine phosphorylase, plus thymidine phosphorylase determined in step (b) is at or below the 20th percentile..

In a further embodiment, in step (b) of the foregoing method the expression level of c-myc and wild-type p53 is determined. In this case, a positive response to 5-FU or an analog thereof is predicted, if the normalized expression level of c-myc relative to the normalized expression level of wild-type p53 is in the upper 15th percentile.

In a still further embodiment, in step (b) of the foregoing method, expression level of NFκB and cIAP2 is determined. In this particular embodiment, resistance to 5-FU or an analog thereof is typically predicted if the normalized expression level of NFκB and cIAP2 is at or above the 10th percentile.

In another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to methotrexate or an analog thereof, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting decreased patient sensitivity to methotrexate or analog if (i) DHFR levels are more than tenfold higher than the average expression level of DHFR in the control gene set, or (ii) the normalized expression levels of members of the reduced folate carrier (RFC) family are below the 10^{th} percentile.

In yet another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to an anthracycline or an analog thereof, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting patient resistance or decreased sensitivity to the anthracycline or analog if (i) the normalized expression level of topoisomerase IIα is below the 10^{th} percentile, or (ii) the normalized expression level of topoisomerase IIβ is below the 10^{th} percentile, or (iii) the combined normalized topoisomerase IIα or IIβ expression levels are below the 10^{th} percentile.

In a different aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to a docetaxol, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting reduced sensitivity to docetaxol if the normalized expression level of CYP1B1 is in the upper 10^{th} percentile.

The invention further concerns a method for predicting the response of a patient diagnosed with breast cancer to cyclophosphamide or an analog thereof, comprising

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting reduced sensitivity to the cyclophosphamide or analog if the sum of the expression levels of aldehyde dehydrogenase 1A1 and 1A3 is more than tenfold higher than the average of their combined expression levels in the reference tissue set.

In a further aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to anti-estrogen therapy, comprising

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set that contains both specimens negative for and positive for estrogen receptor-α (ERα) and progesterone receptor-α (PRα); and

(b) predicting patient response based upon the normalized expression levels of ERα or PRα, and at least one of microsomal epoxide hydrolase, pS2/trefoil factor 1, GATA3 and human chorionic gonadotropin.

In a specific embodiment, lack of response or decreased responsiveness is predicted if (i) the normalized expression level of microsomal epoxide hydrolase is in the upper 10^{th} percentile; or (ii) the normalized expression level of pS2/trefoil factor 1, or GATA3 or human chorionic gonaostropin is at or below the corresponding average expression level in said breast cancer tissue set, regardless of the expression level of ERα or PRα in the breast cancer tissue obtained from the patient.

In another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to a taxane, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting reduced sensitivity to taxane if (i) no or minimal XIST expression is detected; or (ii) the normalized expression level of GST-π or propyl endopeptidase (PREP) is in the upper 10^{th} percentile; or (iii) the normalized expression level of PLAG1 is in the upper 10^{th} percentile.

The invention also concerns a method for predicting the response of a patient diagnosed with breast cancer to cisplatin or an analog thereof, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting resistance or reduced sensitivity if the normalized expression level of ERCC1 is in the upper 10^{th} percentile.

The invention further concerns a method for predicting the response of a patient diagnosed with breast cancer to an ErbB2 or EGFR antagonist, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting patient response based on the normalized expression levels of at least one of Grb7, IGF1R, IGF1 and IGF2.

In particular embodiment, a positive response is predicted if the normalized expression level of Grb7 is in the upper 10^{th} percentile, and the expression of IGF1R, IGF1 and IGF2 is not elevated above the 90^{th} percentile.

In a further particular embodiment, a decreased responsiveness is predicted if the expression level of at least one of IGF1R, IGF1 and IGF2 is elevated.

In another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to a bis-phosphonate drug, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting a positive response if the breast cancer tissue obtained from the patient expresses mutant Ha-Ras and additionally expresses farnesyl pyrophosphate synthetase or geranyl pyrophosphone synthetase at a normalized expression level at or above the 90^{th} percentile.

In yet another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to treatment with a cyclooxygenase 2 inhibitor, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting a positive response if the normalized expression level of COX2 in the breast cancer tissue obtained from the patient is at or above the 90^{th} percentile.

The invention further concerns a method for predicting the response of a patient diagnosed with breast cancer to an EGF receptor (EGFR) antagonist, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting a positive response to an EGFR antagonist, if (i) the normalized expression level of EGFR is at or above the 10^{th} percentile, and (ii) the normalized expression

level of at least one of epiregulin, TGF-α, amphiregulin, ErbB3, BRK, CD9, MMP9, CD82, and Lot1 is above the 90th percentile.

In another aspect, the invention concerns a method for monitoring the response of a patient diagnosed with breast cancer to treatment with an EGFR antagonist, comprising monitoring the expression level of a gene selected from the group consisting of epiregulin, TGF-α, amphiregulin, ErbB3, BRK, CD9, MMP9, CD82, and Lot1 in the patient during treatment, wherein reduction in the expression level is indicative of positive response to such treatment.

In yet another aspect, the invention concerns a method for predicting the response of a patient diagnosed with breast cancer to a drug targeting a tyrosine kinase selected from the group consisting of abl, c-kit, PDGFR-α, PDGFR-β and ARG , comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set;

(b) determining the normalized expression level of a tyrosine kinase selected from the group consisting of abl, c-kit, PDGFR-α, PDGFR-β and ARG, and the cognate ligand of the tyrosine kinase, and if the normalized expression level of the tyrosine kinase is in the upper 10th percentile,

(c) determining whether the sequence of the tyrosine kinase contains any mutation,

wherein a positive response is predicted if (i) the normalized expression level of the tyrosine kinase is in the upper 10th percentile, (ii) the sequence of the tyrosine kinase contains an activating mutation, or (iii) the normalized expression level of the tyrosine kinase is normal and the expression level of the ligand is in the upper 10th percentile.

Another aspect of the invention is a method for predicting the response of a patient diagnosed with breast cancer to treatment with an anti-angiogenic drug, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) predicting a positive response if (i) the normalized expression level of VEGF is in the upper 10th percentile and (ii) the normalized expression level of KDR or CD31 is in the upper 20th percentile.

A further aspect of the invention is a method for predicting the likelihood that a patient diagnosed with breast cancer develops resistance to a drug interacting with the MRP-1 gene coding for the multidrug resistance protein P-glycoprotein, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis to determine the expression level of PTP1b, wherein the expression level is normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) concluding that the patient is likely to develop resistance to said drug if the normalized expression level of the MRP-1 gene is above the 90th percentile.

The invention further relates to a method for predicting the likelihood that a patient diagnosed with breast cancer develops resistance to a chemotherapeutic drug or toxin used in cancer treatment, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) determining the normalized expression levels of at least one of the following genes: MDR1, SGTα, GSTπ, SXR, BCRP YB-1, and LRP/MVP, wherein the finding of a normalized expression level in the upper 4th percentile is an indication that the patient is likely to develop resistance to the drug.

Also included herein is a method for measuring the translational efficiency of VEGF mRNA in a breast cancer tissue sample, comprising determining the expression levels of the VEGF and EIF4E mRNA in the sample, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a higher normalized EIF4E expression level for the same VEGF expression level is indicative of relatively higher translational efficiency for VEGF.

In another aspect, the invention provides a method for predicting the response of a patient diagnosed with breast cancer to a VEGF antagonist, comprising determining the expression level of VEGF and EIF4E mRNA normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a VEGF expression level above the 90th percentile and an EIF4E expression level above the 50th percentile is a predictor of good patient response.

The invention further provides a method for predicting the likelihood of the recurrence of breast cancer in a patient diagnosed with breast cancer, comprising determining the ratio of p53:p21 mRNA expression or p53:mdm2 mRNA expression in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein an above normal ratio is indicative of a higher risk

of recurrence. Typically, a higher risk of recurrence is indicated if the ratio is in the upper 10th percentile.

In yet another aspect, the invention concerns a method for predicting the likelihood of the recurrence of breast cancer in a breast cancer patient following surgery, comprising determining the expression level of cyclin D1 in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein an expression level in the upper 10th percentile indicates increased risk of recurrence following surgery. In a particular embodiment of this method, the patient is subjected to adjuvant chemotherapy, if the expression level is in the upper 10th percentile.

Another aspect of the invention is a method for predicting the likelihood of the recurrence of breast cancer in a breast cancer patient following surgery, comprising determining the expression level of APC or E-cadherin in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein an expression level in the upper 5th percentile indicates high risk of recurrence following surgery, and heightened risk of shortened survival.

A further aspect of the invention is a method for predicting the response of a patient diagnosed with breast cancer to treatment with a proapoptotic drug comprising determining the expression levels of BCl2 and c-MYC in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein (i) a BCl2 expression level in the upper 10th percentile in the absence of elevated expression of c-MYC indicates good response, and (ii) a good response is not indicated if the expression level c-MYC is elevated, regardless of the expression level of BC12.

A still further aspect of the invention is a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising the steps of:

(a) subjecting RNA extracted from a breast cancer tissue obtained from the patient to gene expression analysis, wherein gene expression levels are normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set; and

(b) determining the normalized expression levels of NFκB and at least one gene selected from the group consisting of cIAP1, cIAP2, XIAP, and Survivin,

wherein a poor prognosis is indicated if the expression levels for NFκB and at least one of the genes selected from the group consisting of cIAP1, cIAP2, XIAP, and Survivin is in the upper 5th percentile.

The invention further concerns a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression levels of p53BP1 and p53BP2 in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a poor outcome is predicted if the expression level of either p53BP1 or p53BP2 is in the lower 10^{th} percentile.

The invention additionally concerns a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression levels of uPA and PAI1 in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein (i) a poor outcome is predicted if the expression levels of uPA and PAI1 are in the upper 20^{th} percentile, and (ii) a decreased risk of recurrence is predicted if the expression levels of uPA and PAI1 are not elevated above the mean observed in the breast cancer reference set. In a particular embodiment, poor outcome is measured in terms of shortened survival or increased risk of cancer recurrence following surgery. In another particular embodiment, uPA and PAI1 are expressed at normal levels, and the patient is subjected to adjuvant chemotherapy following surgery.

Another aspect of the invention is a method for predicting treatment outcome in a patient diagnosed with breast cancer, comprising determining the expression levels of cathepsin B and cathepsin L in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a poor outcome is predicted if the expression level of either cathepsin B or cathepsin L is in the upper 10^{th} percentile. Just as before, poor treatment outcome may be measured, for example, in terms of shortened survival or increased risk of cancer recurrence.

A further aspect of the invention is a method for devising the treatment of a patient diagnosed with breast cancer, comprising the steps of

(a) determining the expression levels of scatter factor and c-met in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, and

(b) suggesting prompt aggressive chemotherapeutic treatment if the expression levels of scatter factor and c-met or the combination of both, are above the 90^{th} percentile.

A still further aspect of the invention is a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression levels of VEGF, CD31, and KDR in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein

a poor treatment outcome is predicted if the expression level of any of VEGF, CD31, and KDR is in the upper 10^{th} percentile.

Yet another aspect of the invention is a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression levels of Ki67/MiB1, PCNA, Pin1, and thymidine kinase in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a poor treatment outcome is predicted if the expression level of any of Ki67/MiB1, PCNA, Pin1, and thymidine kinase is in the upper 10^{th} percentile.

The invention further concerns a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression level of soluble and full length CD95 in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein the presence of soluble CD95 correlates with poor patient survival.

The invention also concerns a method for predicting treatment outcome for a patient diagnosed with breast cancer, comprising determining the expression levels of IGF1, IGF1R and IGFBP3 in a breast cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein a poor treatment outcome is predicted if the sum of the expression levels of IGF1, IGF1R and IGFBP3 is in the upper 10^{th} percentile.

The invention additionally concerns a method for classifying breast cancer comprising, determining the expression level of two or more genes selected from the group consisting of Bcl12, hepatocyte nuclear factor 3, LIV1, ER, lipoprotein lipase, retinol binding protein 4, integrin $\alpha 7$, cytokeratin 5, cytokeratin 17, GRO oncogen, ErbB2 and Grb7, in a breast cancer tissue, normalized against a control gene or genes, and compared to the amount found in a reference breast cancer tissue set, wherein (i) tumors expressing at least one of Bcl1, hepatocyte nuclear factor 3, LIV1, and ER above the mean expression level in the reference tissue set are classified as having a good prognosis for disease free and overall patient survival following surgical removal; (ii) tumors characterized by elevated expression of at least one of lipoprotein lipase, retinol binding protein 4, integrin $\alpha 7$ compared to the reference tissue set are classified as having intermediate prognosis of disease free and overall patient survival following surgical removal; and (iii) tumors expressing either elevated levels of cytokeratins 5 and 17, and GRO oncogen at levels four-fold or greater above the mean expression level in the reference tissue set, or ErbB2 and Grb7 at levels ten-fold or more above the mean expression level in the reference

tissue set are classified as having poor prognosis of disease free and overall patient survival following surgical removal.

Another aspect of the invention is a panel of two or more gene specific primers selected from the group consisting of the forward and reverse primers listed in Table 2.

Yet another aspect of the invention is a method for reverse transcription of a fragmented RNA population in RT-PCR amplification, comprising using a multiplicity of gene specific primers as the reverse primers in the amplification reaction. In a particular embodiment, the method uses between two and about 40,000 gene specific primers in the same amplification reaction. In another embodiment, the gene specific primers are about 18 to 24 bases, such as about 20 bases in length. In another embodiment, the Tm of the primers is about 58-60 °C. The primers can, for example, be selected from the group consisting of the forward and reverse primers listed in Table 2.

The invention also concerns a method of reverse transcriptase driven first strand cDNA synthesis, comprising using a gene specific primer of about 18 to 24 bases in length and having a Tm optimum between about 58 °C and about 60 °C. In a particular embodiment, the first strand cDNA synthesis is followed by PCR DNA amplification, and the primer serves as the reverse primer that drives the PCR amplification. In another embodiment, the method uses a plurality of gene specific primers in the same first strand cDNA synthesis reaction mixture. The number of the gene specific primers can, for example, be between 2 and about 40,000.

In a different aspect, the invention concerns a method of predicting the likelihood of long-term survival of a breast cancer patient without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising determining the expression level of one or more prognostic RNA transcripts or their product in a breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products, wherein the prognostic transcript is the transcript of one or more genes selected from the group consisting of: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, CA9, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, GSTM3, RPS6KB1, Src, Chk1, ID1, EstR1, p27, CCNB1, XIAP, Chk2, CDC25B, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, CYP3A4, EpCAM, VEGFC, pS2, hENT1, WISP1, HNF3A, NFKBp65, BRCA2, EGFR, TK1, VDR, Contig51037, pENT1, EPHX1, IF1A, DIABLO, CDH1, HIF1α, IGFBP3, CTSB, and Her2, wherein overexpression of one or more of FOXM1, PRAME, STK15, Ki-67, CA9, NME1, SURV, TFRC, YB-1, RPS6KB1, Src, Chk1, CCNB1, Chk2, CDC25B, CYP3A4, EpCAM, VEGFC, hENT1, BRCA2, EGFR, TK1, VDR, EPHX1, IF1A, Contig51037, CDH1, HIF1α,

IGFBP3, CTSB, Her2, and pENT1 indicates a decreased likelihood of long-term survival without breast cancer recurrence, and the overexpression of one or more of Bcl2, CEGP1, GSTM1, PR, BBC3, GATA3, DPYD, GSTM3, ID1, EstR1, p27, XIAP, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, pS2, WISP1, HNF3A, NFKBp65, and DIABLO indicates an increased likelihood of long-term survival without breast cancer recurrence.

In a particular embodiment of this method, the expression level of at least 2, preferably at least 5, more preferably at least 10, most preferably at least 15 prognostic transcipts or their expression products is determined.

When the breast cancer is invasive breast carcinoma, including both estrogen receptor (ER) overexpressing (ER positive) and ER negative tumors, the analysis includes determination of the expression levels of the transcripts of at least two of the following genes, or their expression products: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, Src, CA9, Contig51037, RPS6K1 and Her2.

When the breast cancer is ER positive invasive breast carcinoma, the analysis includes dtermination of the expression levels of the transcripts of at least two of the following genes, or their expression products: PRAME, Bcl2, FOXM1, DIABLO, EPHX1, HIF1A, VEGFC, Ki-67, IGF1R, VDR, NME1, GSTM3, Contig51037, CDC25B, CTSB, p27, CDH1, and IGFBP3.

Just as before, it is preferred to determine the expression levels of at least 5, more preferably at least 10, most preferably at least 15 genes, or their respective expression products.

In a particular embodiment, the expression level of one or more prognostic RNA transcripts is determined, where RNA may, for example, be obtained from a fixed, wax-embedded breast cancer tissue specimen of the patient. The isolation of RNA can, for example, be carried out following any of the procedures described above or throughout the application, or by any other method known in the art.

In yet another aspect, the invention concerns an array comprising polynucleotides hybridizing to the following genes: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, CA9, Contig51037, RPS6K1 and Her2, immobilized on a solid surface.

In a particular embodiment, the array comprosies polynucleotides hybridizing to the following genes: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, CA9, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, GSTM3, RPS6KB1, Src, Chk1, ID1, EstR1, p27, CCNB1, XIAP, Chk2, CDC25B, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, CYP3A4, EpCAM, VEGFC, pS2, hENT1, WISP1, HNF3A, NFKBp65, BRCA2, EGFR, TK1, VDR, Contig51037, pENT1, EPHX1, IF1A, CDH1, HIF1α, IGFBP3, CTSB, Her2 and DIABLO.

In a further aspect, the invention concerns a method of predicting the likelihood of long-term survival of a patient diagnosed with invasive breast cancer, without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising the steps of:

(1) determining the expression levels of the RNA transcripts or the expression products of genes of a gene set selected from the group consisting of

(a) Bcl2, cyclinG1, NFKBp65, NME1, EPHX1, TOP2B, DR5, TERC, Src, DIABLO;

(b) Ki67, XIAP, hENT1, TS, CD9, p27, cyclinG1, pS2, NFKBp65, CYP3A4;

(c) GSTM1, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, NFKBp65, ErbB3;

(d) PR, NME1, XIAP, upa, cyclinG1, Contig51037, TERC, EPHX1, ALDH1A3, CTSL;

(e) CA9, NME1, TERC, cyclinG1, EPHX1, DPYD, Src, TOP2B, NFKBp65, VEGFC;

(f) TFRC, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, ErbB3, NFKBp65;

(g) Bcl2, PRAME, cyclinG1, FOXM1, NFKBp65, TS, XIAP, Ki67, CYP3A4, p27;

(h) FOXM1, cyclinG1, XIAP, Contig51037, PRAME, TS, Ki67, PDGFRa, p27, NFKBp65;

(i) PRAME, FOXM1, cyclinG1, XIAP, Contig51037, TS, Ki6, PDGFRa, p27, NFKBp65;

(j) Ki67, XIAP, PRAME, hENT1, contig51037, TS, CD9, p27, ErbB3, cyclinG1;

(k) STK15, XIAP, PRAME, PLAUR, p27, CTSL, CD18, PREP, p53, RPS6KB1;

(l) GSTM1, XIAP, PRAME, p27, Contig51037, ErbB3, GSTp, EREG, ID1, PLAUR;

(m) PR, PRAME, NME1, XIAP, PLAUR, cyclinG1, Contig51037, TERC, EPHX1, DR5;

(n) CA9, FOXM1, cyclinG1, XIAP, TS, Ki67, NFKBp65, CYP3A4, GSTM3, p27;

(o) TFRC, XIAP, PRAME, p27, Contig51037, ErbB3, DPYD, TERC, NME1, VEGFC; and

(p) CEGP1, PRAME, hENT1, XIAP, Contig51037, ErbB3, DPYD, NFKBp65, ID1, TS

in a breast cancer tissue sample obtained from said patient, normalized against the expression levels of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products;

(2) subjecting the data obtained in step (a) to statistical analysis; and

(3) determining whether the likelihood of said long-term survival has increased or decreased.

In a still further aspect, the invention concerns a method of predicting the likelihood of long-term survival of a patient diagnosed with estrogen receptor (ER)-positive invasive breast cancer, without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising the steps of:

(1) determining the expression levels of the RNA transcripts or the expression products of genes of a gene set selected from the group consisting of

(a) PRAME, p27, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(b) Contig51037, EPHX1, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(c) Bcl2, hENT1, FOXM1, Contig51037, cyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(d) HIF1A, PRAME, p27, IGFBP2, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(e) IGF1R, PRAME, EPHX1, Contig51037, cyclinG1, Bcl2, NME1, PTEN, TBP, TIMP2;

(f) FOXM1, Contig51037, VEGFC, TBP, HIF1A, DPYD, RAD51C, DCR3, cyclinG1, BAG1;

(g) EPHX1, Contig51037, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(h) Ki67, VEGFC, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(i) CDC25B, Contig51037, hENT1, Bcl2, HLAG, TERC, NME1, upa, ID1, CYP;

(j) VEGFC, Ki67, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(k) CTSB, PRAME, p27, IGFBP2, EPHX1, CTSL, BAD, DR5, DCR3, XIAP;

(l) DIABLO, Ki67, hENT1, TIMP2, ID1, p27, KRT19, IGFBP2, TS, PDGFB;

(m) p27, PRAME, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(n) CDH1; PRAME, VEGFC; HIF1A; DPYD, TIMP2, CYP3A4, EstR1, RBP4, p27;

(o) IGFBP3, PRAME, p27, Bcl2, XIAP, EstR1, Ki67, TS, Src, VEGF;

(p) GSTM3, PRAME, p27, IGFBP3, XIAP, FGF2, hENT1, PTEN, EstR1, APC;

(q) hENT1, Bcl2, FOXM1, Contig51037, CyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(r) STK15, VEGFC, PRAME, p27, GCLC, hENT1, ID1, TIMP2, EstR1, MCP1;

(s) NME1, PRAM, p27, IGFBP3, XIAP, PTEN, hENT1, Bcl2, CYP3A4, HLAG;

(t) VDR, Bcl2, p27, hENT1, p53, PI3KC2A, EIF4E, TFRC, MCM3, ID1;

(u) EIF4E, Contig51037, EPHX1, cyclinG1, Bcl2, DR5, TBP, PTEN, NME1, HER2;

(v) CCNB1, PRAME, VEGFC, HIF1A, hENT1, GCLC, TIMP2, ID1, p27, upa;

(w) ID1, PRAME, DIABLO, hENT1, p27, PDGFRa, NME1, BIN1, BRCA1, TP;

(x) FBXO5, PRAME, IGFBP3, p27, GSTM3, hENT1, XIAP, FGF2, TS, PTEN;

(y) GUS, HIA1A, VEGFC, GSTM3, DPYD, hENT1, EBXO5, CA9, CYP, KRT18; and

(z) Bclx, Bcl2, hENT1, Contig51037, HLAG, CD9, ID1, BRCA1, BIN1, HBEGF;

(2) subjecting the data obtained in step (1) to statistical analysis; and

(3) determining whether the likelihood of said long-term survival has increased or decreased.

In a different aspect, the invention concerns an array comprising polynucleotides hybridizing to a gene set selected from the group consisting of:

(a) Bcl2, cyclinG1, NFKBp65, NME1, EPHX1, TOP2B, DR5, TERC, Src, DIABLO;

(b) Ki67, XIAP, hENT1, TS, CD9, p27, cyclinG1, pS2, NFKBp65, CYP3A4;

(c) GSTM1, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, NFKBp65, ErbB3;

(d) PR, NME1, XIAP, upa, cyclinG1, Contig51037, TERC, EPHX1, ALDH1A3, CTSL;

(e) CA9, NME1, TERC, cyclinG1, EPHX1, DPYD, Src, TOP2B, NFKBp65, VEGFC;

(f) TFRC, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, ErbB3, NFKBp65;

(g) Bcl2, PRAME, cyclinG1, FOXM1, NFKBp65, TS, XIAP, Ki67, CYP3A4, p27;

(h) FOXM1, cyclinG1, XIAP, Contig51037, PRAME, TS, Ki67, PDGFRa, p27, NFKBp65;

(i) PRAME, FOXM1, cyclinG1, XIAP, Contig51037, TS, Ki6, PDGFRa, p27, NFKBp65;

(j) Ki67, XIAP, PRAME, hENT1, contig51037, TS, CD9, p27, ErbB3, cyclinG1;

(k) STK15, XIAP, PRAME, PLAUR, p27, CTSL, CD18, PREP, p53, RPS6KB1;

(l) GSTM1, XIAP, PRAME, p27, Contig51037, ErbB3, GSTp, EREG, ID1, PLAUR;

(m) PR, PRAME, NME1, XIAP, PLAUR, cyclinG1, Contig51037, TERC, EPHX1, DR5;

(n) CA9, FOXM1, cyclinG1, XIAP, TS, Ki67, NFKBp65, CYP3A4, GSTM3, p27;

(o) TFRC, XIAP, PRAME, p27, Contig51037, ErbB3, DPYD, TERC, NME1, VEGFC; and

(p) CEGP1, PRAME, hENT1, XIAP, Contig51037, ErbB3, DPYD, NFKBp65, ID1, TS,

immobilized on a solid surface.

In an additional aspect, the invention concerns an array comprising polynucleotides hybridizing to a gene set selected from the group consisting of:

(a) PRAME, p27, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(b) Contig51037, EPHX1, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(c) Bcl2, hENT1, FOXM1, Contig51037, cyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(d) HIF1A, PRAME, p27, IGFBP2, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(e) IGF1R, PRAME, EPHX1, Contig51037, cyclinG1, Bcl2, NME1, PTEN, TBP, TIMP2;

(f) FOXM1, Contig51037, VEGFC, TBP, HIF1A, DPYD, RAD51C, DCR3, cyclinG1, BAG1;

(g) EPHX1, Contig51037, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(h) Ki67, VEGFC, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(i) CDC25B, Contig51037, hENT1, Bcl2, HLAG, TERC, NME1, upa, ID1, CYP;

(j) VEGFC, Ki67, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(k) CTSB, PRAME, p27, IGFBP2, EPHX1, CTSL, BAD, DR5, DCR3, XIAP;

(l) DIABLO, Ki67, hENT1, TIMP2, ID1, p27, KRT19, IGFBP2, TS, PDGFB;

(m) p27, PRAME, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(n) CDH1; PRAME, VEGFC; HIF1A; DPYD, TIMP2, CYP3A4, EstR1, RBP4, p27;

(o) IGFBP3, PRAME, p27, Bcl2, XIAP, EstR1, Ki67, TS, Src, VEGF;

(p) GSTM3, PRAME, p27, IGFBP3, XIAP, FGF2, hENT1, PTEN, EstR1, APC;

(q) hENT1, Bcl2, FOXM1, Contig51037, CyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(r) STK15, VEGFC, PRAME, p27, GCLC, hENT1, ID1, TIMP2, EstR1, MCP1;

(s) NME1, PRAM, p27, IGFBP3, XIAP, PTEN, hENT1, Bcl2, CYP3A4, HLAG;

(t) VDR, Bcl2, p27, hENT1, p53, PI3KC2A, EIF4E, TFRC, MCM3, ID1;

(u) EIF4E, Contig51037, EPHX1, cyclinG1, Bcl2, DR5, TBP, PTEN, NME1, HER2;

(v) CCNB1, PRAME, VEGFC, HIF1A, hENT1, GCLC, TIMP2, ID1, p27, upa;

(w) ID1, PRAME, DIABLO, hENT1, p27, PDGFRa, NME1, BIN1, BRCA1, TP;

(x) FBXO5, PRAME, IGFBP3, p27, GSTM3, hENT1, XIAP, FGF2, TS, PTEN;

(y) GUS, HIA1A, VEGFC, GSTM3, DPYD, hENT1, FBXO5, CA9, CYP, KRT18; and

(z) Bclx, Bcl2, hENT1, Contig51037, HLAG, CD9, ID1, BRCA1, BIN1, HBEGF,

immobilized on a solid surface.

In all aspects, the polynucleotides can be cDNAs ("cDNA arrays") that are typically about 500 to 5000 bases long, although shorter or longer cDNAs can also be used and are within the scope of this invention. Alternatively, the polynucleotids can be oligonucleotides (DNA microarrays), which are typically about 20 to 80 bases long, although shorter and longer oligonucleotides are also suitable and are within the scope of the invention. The solid surface can, for example, be glass or nylon, or any other solid surface typically used in preparing arrays, such as microarrays, and is typically glass.

Brief Description of the Drawings

Figure 1 is a chart illustrating the overall workflow of the process of the invention for measurement of gene expression. In the Figure, FPET stands for "fixed paraffin-embedded tissue," and "RT-PCR" stands for "reverse transcriptase PCR." RNA concentration is determined by using the commercial RiboGreen™ RNA Quantitation Reagent and Protocol.

Figure 2 is a flow chart showing the steps of an RNA extraction method according to the invention alongside a flow chart of a representative commercial method.

Figure 3 is a scheme illustrating the steps of an improved method for preparing fragmented mRNA for expression profiling analysis.

Figure 4 illustrates methods for amplification of RNA prior to RT-PCR.

Figure 5 illustrates an alternative scheme for repair and amplification of fragmented mRNA.

Figure 6 shows the measurement of estrogen receptor mRNA levels in 40 FPE breast cancer specimens via RT-PCR. Three 10 micron sections were used for each measurement. Each data point represents the average of triplicate measurements.

Figure 7 shows the results of the measurement of progesterone receptor mRNA levels in 40 FPE breast cancer specimens via RT-PCR performed as described in the legend of Figure 6 above.

Figure 8 shows results from an IVT/RT-PCR experiment.

Figure 9 is a representation of the expression of 92 genes across 70 FPE breast cancer specimens. The y-axis shows expression as cycle threshold times. These genes are a subset of the genes listed in Table 1.

Table 1 shows a breast cancer gene list.

Table 2 sets forth amplicon and primer sequences used for amplification of fragmented mRNA.

Table 3 shows the Accession Nos. and SEQ ID NOS of the breast cance genes examined.

Detailed Description of the Preferred Embodiment

A. Definitions

Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Singleton *et al.*, Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, NY 1994), and March, Advanced Organic Chemistry Reactions, Mechanisms

and Structure 4th ed., John Wiley & Sons (New York, NY 1992), provide one skilled in the art with a general guide to many of the terms used in the present application.

One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described. For purposes of the present invention, the following terms are defined below.

The term "microarray" refers to an ordered arrangement of hybridizable array elements, preferably polynucleotide probes, on a substrate.

The term "polynucleotide," when used in singular or plural, generally refers to any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. Thus, for instance, polynucleotides as defined herein include, without limitation, single- and double-stranded DNA, DNA including single- and double-stranded regions, single- and double-stranded RNA, and RNA including single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or include single- and double-stranded regions. In addition, the term "polynucleotide" as used herein refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The strands in such regions may be from the same molecule or from different molecules. The regions may include all of one or more of the molecules, but more typically involve only a region of some of the molecules. One of the molecules of a triple-helical region often is an oligonucleotide. The term "polynucleotide" specifically includes DNAs and RNAs that contain one or more modified bases. Thus, DNAs or RNAs with backbones modified for stability or for other reasons are "polynucleotides" as that term is intended herein. Moreover, DNAs or RNAs comprising unusual bases, such as inosine, or modified bases, such as tritiated bases, are included within the term "polynucleotides" as defined herein. In general, the term "polynucleotide" embraces all chemically, enzymatically and/or metabolically modified forms of unmodified polynucleotides, as well as the chemical forms of DNA and RNA characteristic of viruses and cells, including simple and complex cells.

The term "oligonucleotide" refers to a relatively short polynucleotide, including, without limitation, single-stranded deoxyribonucleotides, single- or double-stranded ribonucleotides, RNA:DNA hybrids and double-stranded DNAs. Oligonucleotides, such as single-stranded DNA probe oligonucleotides, are often synthesized by chemical methods, for example using automated oligonucleotide synthesizers that are commercially available. However, oligonucleotides can be made by a variety of other methods, including *in vitro* recombinant DNA-mediated techniques and by expression of DNAs in cells and organisms.

The terms "differentially expressed gene," "differential gene expression" and their synonyms, which are used interchangeably, refer to a gene whose expression is activated to a higher or lower level in a subject suffering from a disease, specifically cancer, such as breast cancer, relative to its expression in a normal or control subject. The terms also include genes whose expression is activated to a higher or lower level at different stages of the same disease. It is also understood that a differentially expressed gene may be either activated or inhibited at the nucleic acid level or protein level, or may be subject to alternative splicing to result in a different polypeptide product. Such differences may be evidenced by a change in mRNA levels, surface expression, secretion or other partitioning of a polypeptide, for example. Differential gene expression may include a comparison of expression between two or more genes, or a comparison of the ratios of the expression between two or more genes, or even a comparison of two differently processed products of the same gene, which differ between normal subjects and subjects suffering from a disease, specifically cancer, or between various stages of the same disease. Differential expression includes both quantitative, as well as qualitative, differences in the temporal or cellular expression pattern in a gene or its expression products among, for example, normal and diseased cells, or among cells which have undergone different disease events or disease stages. For the purpose of this invention, "differential gene expression" is considered to be present when there is at least an about two-fold, preferably at least about four-fold, more preferably at least about six-fold, most preferably at least about ten-fold difference between the expression of a given gene in normal and diseased subjects, or in various stages of disease development in a diseased subject.

The phrase "gene amplification" refers to a process by which multiple copies of a gene or gene fragment are formed in a particular cell or cell line. The duplicated region (a stretch of amplified DNA) is often referred to as "amplicon." Usually, the amount of the messenger RNA (mRNA) produced, *i.e.*, the level of gene expression, also increases in the proportion of the number of copies made of the particular gene expressed.

The term "prognosis" is used herein to refer to the prediction of the likelihood of cancer-attributable death or progression, including recurrence, metastatic spread, and drug resistance, of a neoplastic disease, such as breast cancer. The term "prediction" is used herein to refer to the likelihood that a patient will respond either favorably or unfavorably to a drug or set of drugs, and also the extent of those responses. The predictive methods of the present invention can be used clinically to make treatment decisions by choosing the most appropriate treatment modalities for any particular patient. The predictive methods of the present invention are valuable tools in predicting if a patient is likely to respond favorably to a treatment regimen, such

as surgical intervention, chemotherapy with a given drug or drug combination, and/or radiation therapy.

The term "increased resistance" to a particular drug or treatment option, when used in accordance with the present invention, means decreased response to a standard dose of the drug or to a standard treatment protocol.

The term "decreased sensitivity" to a particular drug or treatment option, when used in accordance with the present invention, means decreased response to a standard dose of the drug or to a standard treatment protocol, where decreased response can be compensated for (at least partially) by increasing the dose of drug, or the intensity of treatment.

"Patient response" can be assessed using any endpoint indicating a benefit to the patient, including, without limitation, (1) inhibition, to some extent, of tumor growth, including slowing down and complete growth arrest; (2) reduction in the number of tumor cells; (3) reduction in tumor size; (4) inhibition (i.e., reduction, slowing down or complete stopping) of tumor cell infiltration into adjacent peripheral organs and/or tissues; (5) inhibition (i.e. reduction, slowing down or complete stopping) of metastasis; (6) enhancement of anti-tumor immune response, which may, but does not have to, result in the regression or rejection of the tumor; (7) relief, to some extent, of one or more symptoms associated with the tumor; (8) increase in the length of survival following treatment; and/or (9) decreased mortality at a given point of time following treatment.

The term “treatment” refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented. In tumor (*e.g.*, cancer) treatment, a therapeutic agent may directly decrease the pathology of tumor cells, or render the tumor cells more susceptible to treatment by other therapeutic agents, *e.g.*, radiation and/or chemotherapy.

The term "tumor," as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues.

The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Examples of cancer include but are not limited to, breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer.

The "pathology" of cancer includes all phenomena that compromise the well-being of the patient. This includes, without limitation, abnormal or uncontrollable cell growth, metastasis, interference with the normal functioning of neighboring cells, release of cytokines or other secretory products at abnormal levels, suppression or aggravation of inflammatory or immunological response, neoplasia, premalignancy, malignancy, invasion of surrounding or distant tissues or organs, such as lymph nodes, etc.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, typically: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent that those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x

Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

In the context of the present invention, reference to "at least one," "at least two," "at least five," etc. of the genes listed in any particular gene set means any one or any and all combinations of the genes listed.

The terms "splicing" and "RNA splicing" are used interchangeably and refer to RNA processing that removes introns and joins exons to produce mature mRNA with continuous coding sequence that moves into the cytoplasm of an eukaryotic cell.

In theory, the term "exon" refers to any segment of an interrupted gene that is represented in the mature RNA product (B. Lewin. <u>Genes IV</u> Cell Press, Cambridge Mass. 1990). In theory the term "intron" refers to any segment of DNA that is transcribed but removed from within the transcript by splicing together the exons on either side of it. Operationally, exon sequences occur in the mRNA sequence of a gene as defined by Ref. Seq ID numbers. Operationally, intron sequences are the intervening sequences within the genomic DNA of a gene, bracketed by exon sequences and having GT and AG splice consensus sequences at their 5' and 3' boundaries.

B. <u>Detailed Description</u>

The practice of the present invention will employ, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, and biochemistry, which are within the skill of the art. Such techniques are explained fully in the literature, such as, "Molecular Cloning: A Laboratory Manual", 2nd edition (Sambrook et al., 1989); "Oligonucleotide Synthesis" (M.J. Gait, ed., 1984); "Animal Cell Culture" (R.I. Freshney, ed., 1987); "Methods in Enzymology" (Academic Press, Inc.); "Handbook of Experimental Immunology", 4th edition (D.M. Weir & C.C. Blackwell, eds., Blackwell Science Inc., 1987); "Gene Transfer Vectors for Mammalian Cells" (J.M. Miller & M.P. Calos, eds., 1987); "Current Protocols in Molecular Biology" (F.M. Ausubel et al., eds., 1987); and "PCR: The Polymerase Chain Reaction", (Mullis et al., eds., 1994).

1. <u>*Gene Expression Profiling*</u>

In general, methods of gene expression profiling can be divided into two large groups: methods based on hybridization analysis of polynucleotides, and methods based on sequencing of polynucleotides. The most commonly used methods known in the art for the quantification of mRNA expression in a sample include northern blotting and *in situ* hybridization (Parker & Barnes, *Methods in Molecular Biology* 106:247-283 (1999)); RNAse protection assays (Hod,

Biotechniques 13:852-854 (1992)); and reverse transcription polymerase chain reaction (RT-PCR) (Weis *et al., Trends in Genetics* 8:263-264 (1992)). Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. Representative methods for sequencing-based gene expression analysis include Serial Analysis of Gene Expression (SAGE), and gene expression analysis by massively parallel signature sequencing (MPSS).

2. <u>Reverse Transcriptase PCR (RT-PCR)</u>

Of the techniques listed above, the most sensitive and most flexible quantitative method is RT-PCR, which can be used to compare mRNA levels in different sample populations, in normal and tumor tissues, with or without drug treatment, to characterize patterns of gene expression, to discriminate between closely related mRNAs, and to analyze RNA structure.

The first step is the isolation of mRNA from a target sample. The starting material is typically total RNA isolated from human tumors or tumor cell lines, and corresponding normal tissues or cell lines, respectively. Thus RNA can be isolated from a variety of primary tumors, including breast, lung, colon, prostate, brain, liver, kidney, pancreas, spleen, thymus, testis, ovary, uterus, etc., tumor, or tumor cell lines, with pooled DNA from healthy donors. If the source of mRNA is a primary tumor, mRNA can be extracted, for example, from frozen or archived paraffin-embedded and fixed (e.g. formalin-fixed) tissue samples.

General methods for mRNA extraction are well known in the art and are disclosed in standard textbooks of molecular biology, including Ausubel *et al.*, <u>Current Protocols of Molecular Biology</u>, John Wiley and Sons (1997). Methods for RNA extraction from paraffin embedded tissues are disclosed, for example, in Rupp and Locker, *Lab Invest.* 56:A67 (1987), and De Andrés *et al., BioTechniques* 18:42044 (1995). In particular, RNA isolation can be performed using purification kit, buffer set and protease from commercial manufacturers, such as Qiagen, according to the manufacturer's instructions. For example, total RNA from cells in culture can be isolated using Qiagen RNeasy mini-columns. Other commercially available RNA isolation kits include MasterPure™ Complete DNA and RNA Purification Kit (EPICENTRE®, Madison, WI), and Paraffin Block RNA Isolation Kit (Ambion, Inc.). Total RNA from tissue samples can be isolated using RNA Stat-60 (Tel-Test). RNA prepared from tumor can be isolated, for example, by cesium chloride density gradient centrifugation.

As RNA cannot serve as a template for PCR, the first step in gene expression profiling by RT-PCR is the reverse transcription of the RNA template into cDNA, followed by its exponential amplification in a PCR reaction. The two most commonly used reverse transcriptases are avilo myeloblastosis virus reverse transcriptase (AMV-RT) and Moloney murine leukemia virus

reverse transcriptase (MMLV-RT). The reverse transcription step is typically primed using specific primers, random hexamers, or oligo-dT primers, depending on the circumstances and the goal of expression profiling. For example, extracted RNA can be reverse-transcribed using a GeneAmp RNA PCR kit (Perkin Elmer, CA, USA), following the manufacturer's instructions. The derived cDNA can then be used as a template in the subsequent PCR reaction.

Although the PCR step can use a variety of thermostable DNA-dependent DNA polymerases, it typically employs the Taq DNA polymerase, which has a 5'-3' nuclease activity but lacks a 3'-5' proofreading endonuclease activity. Thus, TaqMan® PCR typically utilizes the 5'-nuclease activity of Taq or Tth polymerase to hydrolyze a hybridization probe bound to its target amplicon, but any enzyme with equivalent 5' nuclease activity can be used. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

TaqMan® RT-PCR can be performed using commercially available equipment, such as, for example, ABI PRISM 7700™ Sequence Detection System™ (Perkin-Elmer-Applied Biosystems, Foster City, CA, USA), or Lightcycler (Roche Molecular Biochemicals, Mannheim, Germany). In a preferred embodiment, the 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI PRISM 7700™ Sequence Detection System™. The system consists of a thermocycler, laser, charge-coupled device (CCD), camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5'-Nuclease assay data are initially expressed as Ct, or the threshold cycle. As discussed above, fluorescence values are recorded during every cycle and represent the amount of product

amplified to that point in the amplification reaction. The point when the fluorescent signal is first recorded as statistically significant is the threshold cycle (C_t).

To minimize errors and the effect of sample-to-sample variation, RT-PCR is usually performed using an internal standard. The ideal internal standard is expressed at a constant level among different tissues, and is unaffected by the experimental treatment. RNAs most frequently used to normalize patterns of gene expression are mRNAs for the housekeeping genes glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) and β-actin.

A more recent variation of the RT-PCR technique is the real time quantitative PCR, which measures PCR product accumulation through a dual-labeled fluorigenic probe (i.e., TaqMan® probe). Real time PCR is compatible both with quantitative competitive PCR, where internal competitor for each target sequence is used for normalization, and with quantitative comparative PCR using a normalization gene contained within the sample, or a housekeeping gene for RT-PCR. For further details see, e.g. Held *et al., Genome Research* 6:986-994 (1996).

3. *Microarrays*

Differential gene expression can also be identified, or confirmed using the microarray technique. Thus, the expression profile of breast cancer-associated genes can be measured in either fresh or paraffin-embedded tumor tissue, using microarray technology. In this method, polynucleotide sequences of interest are plated, or arrayed, on a microchip substrate. The arrayed sequences are then hybridized with specific DNA probes from cells or tissues of interest. Just as in the RT-PCR method, the source of mRNA typically is total RNA isolated from human tumors or tumor cell lines, and corresponding normal tissues or cell lines. Thus RNA can be isolated from a variety of primary tumors or tumor cell lines. If the source of mRNA is a primary tumor, mRNA can be extracted, for example, from frozen or archived paraffin-embedded and fixed (e.g. formalin-fixed) tissue samples, which are routinely prepared and preserved in everyday clinical practice.

In a specific embodiment of the microarray technique, PCR amplified inserts of cDNA clones are applied to a substrate in a dense array. Preferably at least 10,000 nucleotide sequences are applied to the substrate. The microarrayed genes, immobilized on the microchip at 10,000 elements each, are suitable for hybridization under stringent conditions. Fluorescently labeled cDNA probes may be generated through incorporation of fluorescent nucleotides by reverse transcription of RNA extracted from tissues of interest. Labeled cDNA probes applied to the chip hybridize with specificity to each spot of DNA on the array. After stringent washing to remove non-specifically bound probes, the chip is scanned by confocal laser microscopy or by another detection method, such as a CCD camera. Quantitation of hybridization of each arrayed

element allows for assessment of corresponding mRNA abundance. With dual color fluorescence, separately labeled cDNA probes generated from two sources of RNA are hybridized pairwise to the array. The relative abundance of the transcripts from the two sources corresponding to each specified gene is thus determined simultaneously. The miniaturized scale of the hybridization affords a convenient and rapid evaluation of the expression pattern for large numbers of genes. Such methods have been shown to have the sensitivity required to detect rare transcripts, which are expressed at a few copies per cell, and to reproducibly detect at least approximately two-fold differences in the expression levels (Schena *et al., Proc. Natl. Acad. Sci. USA* 93(2):106-149 (1996)). Microarray analysis can be performed by commercially available equipment, following manufacturer's protocols, such as by using the Affymetrix GenChip technology, or Incyte's microarray technology.

The development of microarray methods for large-scale analysis of gene expression makes it possible to search systematically for molecular markers of cancer classification and outcome prediction in a variety of tumor types.

4. *Serial Analysis of Gene Expression (SAGE)*

Serial analysis of gene expression (SAGE) is a method that allows the simultaneous and quantitative analysis of a large number of gene transcripts, without the need of providing an individual hybridization probe for each transcript. First, a short sequence tag (about 10-14 bp) is generated that contains sufficient information to uniquely identify a transcript, provided that the tag is obtained from a unique position within each transcript. Then, many transcripts are linked together to form long serial molecules, that can be sequenced, revealing the identity of the multiple tags simultaneously. The expression pattern of any population of transcripts can be quantitatively evaluated by determining the abundance of individual tags, and identifying the gene corresponding to each tag. For more details see, e.g. Velculescu *et al., Science* 270:484-487 (1995); and Velculescu *et al., Cell* 88:243-51 (1997).

5. *Gene Expression Analysis by Massively Parallel Signature Sequencing (MPSS)*

This method, described by Brenner *et al., Nature Biotechnology* 18:630-634 (2000), is a sequencing approach that combines non-gel-based signature sequencing with *in vitro* cloning of millions of templates on separate 5 μm diameter microbeads. First, a microbead library of DNA templates is constructed by *in vitro* cloning. This is followed by the assembly of a planar array of the template-containing microbeads in a flow cell at a high density (typically greater than 3 x 10^6 microbeads/cm^2). The free ends of the cloned templates on each microbead are analyzed simultaneously, using a fluorescence-based signature sequencing method that does not require DNA fragment separation. This method has been shown to simultaneously and accurately

provide, in a single operation, hundreds of thousands of gene signature sequences from a yeast cDNA library.

6. *General Description of the mRNA Isolation, Purification and Amplification Methods of the Invention*

The steps of a representative protocol of the invention, including mRNA isolation, purification, primer extension and amplification are illustrated in Figure 1. As shown in Figure 1, this representative process starts with cutting about 10 μm thick sections of paraffin-embedded tumor tissue samples. The RNA is then extracted, and protein and DNA are removed, following the method of the invention described below. After analysis of the RNA concentration, RNA repair and/or amplification steps may be included, if necessary, and RNA is reverse transcribed using gene specific promoters followed by RT-PCR. Finally, the data are analyzed to identify the best treatment option(s) available to the patient on the basis of the characteristic gene expression pattern identified in the tumor sample examined. The individual steps of this protocol will be discussed in greater detail below.

7. *Improved Method for Isolation of Nucleic Acid from Archived Tissue Specimens*

As discussed above, in the first step of the method of the invention, total RNA is extracted from the source material of interest, including fixed, paraffin-embedded tissue specimens, and purified sufficiently to act as a substrate in an enzyme assay. Despite the availability of commercial products, and the extensive knowledge available concerning the isolation of nucleic acid, such as RNA, from tissues, isolation of nucleic acid (RNA) from fixed, paraffin-embedded tissue specimens (FPET) is not without difficulty.

In one aspect, the present invention concerns an improved method for the isolation of nucleic acid from archived, e.g. FPET tissue specimens. Measured levels of mRNA species are useful for defining the physiological or pathological status of cells and tissues. RT-PCR (which is discussed above) is one of the most sensitive, reproducible and quantitative methods for this "gene expression profiling". Paraffin-embedded, formalin-fixed tissue is the most widely available material for such studies. Several laboratories have demonstrated that it is possible to successfully use fixed-paraffin-embedded tissue (FPET) as a source of RNA for RT-PCR (Stanta *et al., Biotechniques* 11:304-308 (1991); Stanta *et al., Methods Mol. Biol.* 86:23-26 (1998); Jackson *et al., Lancet* 1:1391 (1989); Jackson *et al., J. Clin. Pathol.* 43:499-504 (1999); Finke *et al., Biotechniques* 14:448-453 (1993); Goldsworthy *et al., Mol. Carcinog.* 25:86-91 (1999); Stanta and Bonin, *Biotechniques* 24:271-276 (1998); Godfrey *et al., J. Mol. Diagnostics* 2:84 (2000); Specht *et al., J. Mol. Med.* 78:B27 (2000); Specht *et al., Am. J. Pathol.* 158:419-429 (2001)). This allows gene expression profiling to be carried out on the most commonly available

source of human biopsy specimens, and therefore potentially to create new valuable diagnostic and therapeutic information.

The most widely used protocols utilize hazardous organic solvents, such as xylene, or octane (Finke *et al., supra*) to dewax the tissue in the paraffin blocks before nucleic acid (RNA and/or DNA) extraction. Obligatory organic solvent removal (e.g. with ethanol) and rehydration steps follow, which necessitate multiple manipulations, and addition of substantial total time to the protocol, which can take up to several days. Commercial kits and protocols for RNA extraction from FPET [MasterPure™ Complete DNA and RNA Purification Kit (EPICENTRE®, Madison, WI); Paraffin Block RNA Isolation Kit (Ambion, Inc.) and RNeasy™ Mini kit (Qiagen, Chatsworth, CA)] use xylene for deparaffinization, in procedures which typically require multiple centrifugations and ethanol buffer changes, and incubations following incubation with xylene.

The present invention provides an improved nucleic acid extraction protocol that produces nucleic acid, in particular RNA, sufficiently intact for gene expression measurements. The key step in the nucleic acid extraction protocol herein is the performance of dewaxing without the use of any organic solvent, thereby eliminating the need for multiple manipulations associated with the removal of the organic solvent, and substantially reducing the total time to the protocol. According to the invention, wax, e.g. paraffin is removed from wax-embedded tissue samples by incubation at 65-75 °C in a lysis buffer that solubilizes the tissue and hydrolyzes the protein, following by cooling to solidify the wax.

Figure 2 shows a flow chart of an RNA extraction protocol of the present invention in comparison with a representative commercial method, using xylene to remove wax. The times required for individual steps in the processes and for the overall processes are shown in the chart. As shown, the commercial process requires approximately 50% more time than the process of the invention.

The lysis buffer can be any buffer known for cell lysis. It is, however, preferred that oligo-dT-based methods of selectively purifying polyadenylated mRNA not be used to isolate RNA for the present invention, since the bulk of the mRNA molecules are expected to be fragmented and therefore will not have an intact polyadenylated tail, and will not be recovered or available for subsequent analytical assays. Otherwise, any number of standard nucleic acid purification schemes can be used. These include chaotrope and organic solvent extractions, extraction using glass beads or filters, salting out and precipitation based methods, or any of the purification methods known in the art to recover total RNA or total nucleic acids from a biological source.

Lysis buffers are commercially available, such as, for example, from Qiagen, Epicentre, or Ambion. A preferred group of lysis buffers typically contains urea, and Proteinase K or other protease. Proteinase K is very useful in the isolation of high quality, undamaged DNA or RNA, since most mammalian DNases and RNases are rapidly inactivated by this enzyme, especially in the presence of 0.5 - 1% sodium dodecyl sulfate (SDS). This is particularly important in the case of RNA, which is more susceptible to degradation than DNA. While DNases require metal ions for activity, and can therefore be easily inactivated by chelating agents, such as EDTA, there is no similar co-factor requirement for RNases.

Cooling and resultant solidification of the wax permits easy separation of the wax from the total nucleic acid, which can be conveniently precipitated, e.g. by isopropanol. Further processing depends on the intended purpose. If the proposed method of RNA analysis is subject to bias by contaminating DNA in an extract, the RNA extract can be further treated, e.g. by DNase, post purification to specifically remove DNA while preserving RNA. For example, if the goal is to isolate high quality RNA for subsequent RT-PCR amplification, nucleic acid precipitation is followed by the removal of DNA, usually by DNase treatment. However, DNA can be removed at various stages of nucleic acid isolation, by DNase or other techniques well known in the art.

While the advantages of the nucleic acid extraction protocol of the invention are most apparent for the isolation of RNA from archived, paraffin embedded tissue samples, the wax removal step of the present invention, which does not involve the use of an organic solvent, can also be included in any conventional protocol for the extraction of total nucleic acid (RNA and DNA) or DNA only. All of these aspects are specifically within the scope of the invention.

By using heat followed by cooling to remove paraffin, the process of the present invention saves valuable processing time, and eliminates a series of manipulations, thereby potentially increasing the yield of nucleic acid. Indeed, experimental evidence presented in the examples below, demonstrates that the method of the present invention does not compromise RNA yield.

8. *5'-multiplexed Gene Specific Priming of Reverse Transcription*

RT-PCR requires reverse transcription of the test RNA population as a first step. The most commonly used primer for reverse transcription is oligo-dT, which works well when RNA is intact. However, this primer will not be effective when RNA is highly fragmented as is the case in FPE tissues.

The present invention includes the use of gene specific primers, which are roughly 20 bases in length with a Tm optimum between about 58 °C and 60 °C. These primers will also serve as the reverse primers that drive PCR DNA amplification.

Another aspect of the invention is the inclusion of multiple gene-specific primers in the same reaction mixture. The number of such different primers can vary greatly and can be as low as two and as high as 40,000 or more. Table 2 displays examples of reverse primers that can be successfully used in carrying out the methods of the invention. Figure 9 shows expression data obtained using this multiplexed gene-specific priming strategy. Specifically, Figure 9 is a representation of the expression of 92 genes (a subset of genes listed in Table 1) across 70 FPE breast cancer specimens. The y-axis shows expression as cycle threshold times.

An alternative approach is based on the use of random hexamers as primers for cDNA synthesis. However, we have experimentally demonstrated that the method of using a multiplicity of gene-specific primers is superior over the known approach using random hexamers.

9. *Preparation of Fragmented mRNA for Expression Profiling Assays*

It is of interest to analyze the abundance of specific mRNA species in biological samples, since this expression profile provides an index of the physiological state of that sample. mRNA is notoriously difficult to extract and maintain in its native state, consequently, mRNA recovered from biological sources is often fragmented or somewhat degraded. This is especially true of human tissue specimen which have been chemically fixed and stored for extended periods of time.

In one aspect, the present invention provides a means of preparing the mRNA extracted from various sources, including archived tissue specimens, for expression profiling in a way that its relative abundance is preserved and the mRNA's of interest can be successfully measured. This method is useful as a means of preparing mRNA for analysis by any of the known expression profiling methods, including RT-PCR coupled with 5' exonuclease of reporter probes (TaqMan® type assays), as discussed above, flap endonuclease assays (Cleavase® and Invader® type assays), oligonucleotide hybridization arrays, cDNA hybridization arrays, oligonucleotide ligation assays, 3' single nucleotide extension assays and other assays designed to assess the abundance of specific mRNA sequences in a biological sample.

According to the method of the invention, total RNA is extracted from the source material and sufficiently purified to act as a substrate in an enzyme assay. The extraction procedure, including a new and improved way of removing the wax (e.g. paraffin) used for embedding the tissue samples, has been discussed above. It has also been noted that it is preferred that oligo-dT based methods of selectively purifying polyadenylated mRNA not be used to isolate RNA for this invention since the bulk of the mRNA is expected to be fragmented, will not be polyadenylated

and, therefore, will not be recovered and available for subsequent analytical assays if an oligo-dT based method is used.

A diagram of an improved method for repairing fragmented RNA is shown in Figure 3. The fragmented RNA purified from the tissue sample is mixed with universal or gene-specific, single-stranded, DNA templates for each mRNA species of interest. These templates may be full length DNA copies of the mRNA derived from cloned gene sources, they may be fragments of the gene representing only the segment of the gene to be assayed, they may be a series of long oligonucleotides representing either the full length gene or the specific segment(s) of interest. The template can represent either a single consensus sequence or be a mixture of polymorphic variants of the gene. This DNA template, or scaffold, will preferably include one or more dUTP or rNTP sites in its length. This will provide a means of removing the template prior to carrying out subsequent analytical steps to avoid its acting as a substrate or target in later analysis assays. This removal is accomplished by treating the sample with uracil-DNA glycosylase (UDG) and heating it to cause strand breaks where UDG has generated abasic sites. In the case of rNTP's, the sample can be heated in the presence of a basic buffer (pH ~10) to induce strand breaks where rNTP's are located in the template.

The single stranded DNA template is mixed with the purified RNA, the mixture is denatured and annealed so that the RNA fragments complementary to the DNA template effectively become primers that can be extended along the single stranded DNA templates. DNA polymerase I requires a primer for extension but will efficiently use either a DNA or an RNA primer. Therefore in the presence of DNA polymerase I and dNTP's, the fragmented RNA can be extended along the complementary DNA templates. In order to increase the efficiency of the extension, this reaction can be thermally cycled, allowing overlapping templates and extension products to hybridize and extend until the overall population of fragmented RNA becomes represented as double stranded DNA extended from RNA fragment primers.

Following the generation of this "repaired" RNA, the sample should be treated with UDG or heat-treated in a mildly based solution to fragment the DNA template (scaffold) and prevent it from participating in subsequent analytical reactions.

The product resulting from this enzyme extension can then be used as a template in a standard enzyme profiling assay that includes amplification and detectable signal generation such as fluorescent, chemiluminescent, colorimetric or other common read outs from enzyme based assays. For example, for TaqMan® type assays, this double stranded DNA product is added as the template in a standard assay; and, for array hybridization, this product acts as the cDNA

template for the cRNA labeling reaction typically used to generate single-stranded, labeled RNA for array hybridization.

This method of preparing template has the advantage of recovering information from mRNA fragments too short to effectively act as templates in standard cDNA generation schemes. In addition, this method acts to preserve the specific locations in mRNA sequences targeted by specific analysis assays. For example, TaqMan® assays rely on a single contiguous sequence in a cDNA copy of mRNA to act as a PCR amplification template targeted by a labeled reporter probe. If mRNA strand breaks occur in this sequence, the assay will not detect that template and will underestimate the quantity of that mRNA in the original sample. This target preparation method minimizes that effect from RNA fragmentation.

The extension product formed in the RNA primer extension assay can be controlled by controlling the input quantity of the single stranded DNA template and by doing limited cycling of the extension reaction. This is important in preserving the relative abundance of the mRNA sequences targeted for analysis.

This method has the added advantage of not requiring parallel preparation for each target sequence since it is easily multiplexed. It is also possible to use large pools of random sequence long oligonucleotides or full libraries of cloned sequences to extend the entire population of mRNA sequences in the sample extract for whole expressed genome analysis rather than targeted gene specific analysis.

10. *Amplification of mRNA Species Prior to RT-PCR*

Due to the limited amount and poor quality of mRNA that can be isolated from FPET, a new procedure that could accurately amplify mRNAs of interest would be very useful, particularly for real time quantitation of gene expression (TaqMan®) and especially for quantitatively large number (>50) of genes >50 to 10,000.

Current protocols (e.g. Eberwine, *Biotechniques* 20:584-91 (1996)) are optimized for mRNA amplification from small amount of total or poly A^+ RNA mainly for microarray analysis. The present invention provides a protocol optimized for amplification of small amounts of fragmented total RNA (average size about 60-150 bps), utilizing gene-specific sequences as primers, as illustrated in Figure 4.

The amplification procedure of the invention uses a very large number, typically as many as 100 - 190,000 gene specific primers (GSP's) in one reverse transcription run. Each GSP contains an RNA polymerase promoter, e.g. a T7 DNA-dependent RNA polymerase promoter, at the 5' end for subsequent RNA amplification. GSP's are preferred as primers because of the small size of the RNA. Current protocols utilize dT primers, which would not adequately

represent all reverse transcripts of mRNAs due to the small size of the FPET RNA. GSP's can be designed by optimizing usual parameters, such as length, Tm, etc. For example, GSP's can be designed using the Primer Express® (Applied Biosystems), or Primer 3 (MIT) software program. Typically at least 3 sets per gene are designed, and the ones giving the lowest Ct on FPET RNA (best performers) are selected.

Second strand cDNA synthesis is performed by standard procedures (see Figure 4, Method 1), or by GSP_f primers and Taq pol under PCR conditions (e.g., 95 °C, 10 min (Taq activation) then 60 °C, 45 sec). The advantages of the latter method are that the second gene specific primer, SGF_f adds additional specificity (and potentially more efficient second strand synthesis) and the option of performing several cycles of PCR, if more starting DNA is necessary for RNA amplification by T7 RNA polymerase. RNA amplification is then performed under standard conditions to generate multiple copies of cRNA, which is then used in a standard TaqMan® reaction.

Although this process is illustrated by using T7-based RNA amplification, a person skilled in the art will understand that other RNA polymerase promoters that do not require a primer, such as T3 or Sp6 can also be used, and are within the scope of the invention.

11. *A method of Elongation of Fragmented RNA and Subsequent Amplification*

This method, which combines and modifies the inventions described in sections 9 and 10 above, is illustrated in Figure 5. The procedure begins with elongation of fragmented mRNA. This occurs as described above except that the scaffold DNAs are tagged with the T7 RNA polymerase promoter sequence at their 5' ends, leading to double-stranded DNA extended from RNA fragments. The template sequences need to be removed after *in vitro* transcription. These templates can include dUTP or rNTP nucleotides, enabling enzymatic removal of the templates as described in section 9, or the templates can be removed by DNaseI treatment.

The template DNA can be a population representing different mRNAs of any number. A high sequence complexity source of DNA templates (scaffolds) can be generated by pooling RNA from a variety of cells or tissues. In one embodiment, these RNAs are converted into double stranded DNA and cloned into phagemids. Single stranded DNA can then be rescued by phagemid growth and single stranded DNA isolation from purified phagemids.

This invention is useful because it increases gene expression profile signals two different ways: both by increasing test mRNA polynucleotide sequence length and by *in vitro* transcription amplification. An additional advantage is that it eliminates the need to carry out reverse transcription optimization with gene specific primers tagged with the T7 RNA polymerase promoter sequence, and thus, is comparatively fast and economical.

This invention can be used with a variety of different methods to profile gene expression, e.g., RT-PCR or a variety of DNA array methods. Just as in the previous protocol, this approach is illustrated by using a T7 promoter but the invention is not so limited. A person skilled in the art will appreciate, however, that other RNA polymerase promoters, such as T3 or Sp6 can also be used.

12. *Breast Cancer Gene Set, Assayed Gene Subsequences, and Clinical Application of Gene Expression Data*

An important aspect of the present invention is to use the measured expression of certain genes by breast cancer tissue to match patients to best drugs or drug combinations, and to provide prognostic information. For this purpose it is necessary to correct for (normalize away) both differences in the amount of RNA assayed and variability in the quality of the RNA used. Therefore, the assay measures and incorporates the expression of certain normalizing genes, including well known housekeeping genes, such as GAPDH and Cyp1. Alternatively, normalization can be based on the mean or median signal (Ct) of all of the assayed genes or a large subset thereof (global normalization approach). On a gene-by-gene basis, measured normalized amount of a patient tumor mRNA is compared to the amount found in a breast cancer tissue reference set. The number (N) of breast cancer tissues in this reference set should be sufficiently high to ensure that different reference sets (as a whole) behave essentially the same way. If this condition is met, the identity of the individual breast cancer tissues present in a particular set will have no significant impact on the relative amounts of the genes assayed. Usually, the breast cancer tissue reference set consists of at least about 30, preferably at least about 40 different FPE breast cancer tissue specimens. Unless noted otherwise, normalized expression levels for each mRNA/tested tumor/patient will be expressed as a percentage of the expression level measured in the reference set. More specifically, the reference set of a sufficiently high number (e.g. 40) tumors yields a distribution of normalized levels of each mRNA species. The level measured in a particular tumor sample to be analyzed falls at some percentile within this range, which can be determined by methods well known in the art. Below, unless noted otherwise, reference to expression levels of a gene assume normalized expression relative to the reference set although this is not always explicitly stated.

The breast cancer gene set is shown in Table 1. The gene Accession Numbers, and the SEQ ID NOs for the forward primer, reverse primer and amplicon sequences that can be used for gene amplification, are listed in Table 2. The basis for inclusion of markers, as well as the clinical significance of mRNA level variations with respect to the reference set, is indicated below. Genes are grouped into subsets based on the type of clinical significance indicated by

their expression levels: A. Prediction of patient response to drugs used in breast cancer treatment, or to drugs that are approved for other indications and could be used off-label in the treatment of breast cancer. B. Prognostic for survival or recurrence of cancer.

C. <u>Prediction of Patient Response to Therapeutic Drugs</u>

1. *<u>Molecules that specifically influence cellular sensitivity to drugs</u>*

Table 1 lists 74 genes (shown in italics) that specifically influence cellular sensitivity to potent drugs, which are also listed. Most of the drugs shown are approved and already used to treat breast cancer (e.g., anthracyclines; cyclophosphamide; methotrexate; 5-FU and analogues). Several of the drugs are used to treat breast cancer off-label or are in clinical development phase (e.g., bisphosphonates and anti-VEGF mAb). Several of the drugs have not been widely used to treat breast cancer but are used in other cancers in which the indicated target is expressed (e.g., Celebrex is used to treat familial colon cancer; cisplatin is used to treat ovarian and other cancers.)

Patient response to 5FU is indicated if normalized thymidylate synthase mRNA amount is at or below the 15^{th} percentile, or the sum of expression of thymidylate synthase plus dihydropyrimidine phosphorylase is at or below the 25^{th} percentile, or the sum of expression of these mRNAs plus thymidine phosphorylase is at or below the 20^{th} percentile. Patients with dihydropyrimidine dehydrogenase below 5^{th} percentile are at risk of adverse response to 5FU, or analogs such as Xeloda.

When levels of thymidylate synthase, and dihydropyrimidine dehydrogenase, are within the acceptable range as defined in the preceding paragraph, amplification of c-myc mRNA in the upper 15%, against a background of wild-type p53 [as defined below] predicts a beneficial response to 5FU (see D. Arango *et al., Cancer Res.* 61:4910-4915 (2001)). In the presence of normal levels of thymidylate synthase and dihydropyrimidine dehydrogenase, levels of NFκB and cIAP2 in the upper 10% indicate resistance of breast tumors to the chemotherapeutic drug 5FU.

Patient resistance to anthracyclines is indicated if the normalized mRNA level of topoisomerase IIα is below the 10^{th} percentile, or if the topoisomerase IIβ normalized mRNA level is below the 10^{th} percentile or if the combined normalized topoisomerase IIα and β signals are below the 10^{th} percentile.

Patient sensitivity to methotrexate is compromised if DHFR levels are more than tenfold higher than the average reference set level for this mRNA species, or if reduced folate carrier levels are below 10^{th} percentile.

Patients whose tumors express CYP1B1 in the upper 10%, have reduced likelihood of responding to docetaxol.

The sum of signals for aldehyde dehydrogenase 1A1 and 1A3, when more than tenfold higher than the reference set average, indicates reduced likelihood of response to cyclophosphamide.

Currently, estrogen and progesterone receptor expression as measured by immunohistochemistry is used to select patients for anti-estrogen therapy. We have demonstrated RT-PCR assays for estrogen and progesterone receptor mRNA levels that predict levels of these proteins as determined by a standard clinical diagnostic tests, with high degree of concordance (Figures 6 and 7).

Patients whose tumors express ERα or PR mRNA in the upper 70%, are likely to respond to tamoxifen or other anti-estrogens (thus, operationally, lower levels of ERα than this are to defined ERα-negative). However, when the signal for microsomal epoxide hydrolase is in the upper 10% or when mRNAs for pS2/trefoil factor, GATA3 or human chorionic gonadotropin are at or below average levels found in ERα-negative tumors, anti-estrogen therapy will not be beneficial.

Absence of XIST signal compromises the likelihood of response to taxanes, as does elevation of the GST-π or prolyl endopeptidase [PREP] signal in the upper 10%. Elevation of PLAG1 in the upper 10% decreases sensitivity to taxanes.

Expression of ERCC1 mRNA in the upper 10% indicate significant risk of resistance to cisplatin or analogs.

An RT-PCR assay of Her2 mRNA expression predicts Her2 overexpression as measured by a standard diagnostic test, with high degree of concordance (data not shown). Patients whose tumors express Her2 (normalized to cyp.1) in the upper 10% have increased likelihood of beneficial response to treatment with Herceptin or other ErbB2 antagonists. Measurement of expression of Grb7 mRNA serves as a test for HER2 gene amplification, because the Grb7 gene is closely linked to Her2. When Her2 is expression is high as defined above in this paragraph, similarly elevated Grb7 indicates Her2 gene amplification. Overexpression of IGF1R and or IGF1 or IGF2 decreases likelihood of beneficial response to Herceptin and also to EGFR antagonists.

Patients whose tumors express mutant Ha-Ras, and also express farnesyl pyrophosphate synthetase or geranyl pyrophosphonate synthetase mRNAs at levels above the tenth percentile comprise a group that is especially likely to exhibit a beneficial response to bis-phosphonate drugs.

Cox2 is a key control enzyme in the synthesis of prostaglandins. It is frequently expressed at elevated levels in subsets of various types of carcinomas including carcinoma of the breast. Expression of this gene is controlled at the transcriptional level, so RT-PCR serves a valid indicator of the cellular enzyme activity. Nonclinical research has shown that cox2 promotes tumor angiogenesis, suggesting that this enzyme is a promising drug target in solid tumors. Several Cox2 antagonists are marketed products for use in anti-inflammatory conditions. Treatment of familial adenomatous polyposis patients with the cox2 inhibitor Celebrex significantly decreased the number and size of neoplastic polyps. No cox2 inhibitor has yet been approved for treatment of breast cancer, but generally this class of drugs is safe and could be prescribed off-label in breast cancers in which cox2 is over-expressed. Tumors expressing COX2 at levels in the upper ten percentile have increased chance of beneficial response to Celebrex or other cyclooxygenase 2 inhibitors.

The tyrosine kinases ErbB1 [EGFR], ErbB3 [Her3] and ErbB4 [Her4]; also the ligands TGFalpha, amphiregulin, heparin-binding EGF-like growth factor, and epiregulin; also BRK, a non-receptor kinase. Several drugs in clinical development block the EGF receptor. ErbB2-4, the indicated ligands, and BRK also increase the activity of the EGFR pathway. Breast cancer patients whose tumors express high levels of EGFR or EGFR and abnormally high levels of the other indicated activators of the EGFR pathway are potential candidates for treatment with an EGFR antagonist.

Patients whose tumors express less than 10% of the average level of EGFR mRNA observed in the reference panel are relatively less likely to respond to EGFR antagonists [such as Iressa, or ImClone 225]. In cases in which the EGFR is above this low range, the additional presence of epiregulin, TGFα, amphiregulin, or ErbB3, or BRK, CD9, MMP9, or Lot1 at levels above the 90th percentile predisposes to response to EGFR antagonists. Epiregulin gene expression, in particular, is a good surrogate marker for EGFR activation, and can be used to not only to predict response to EGFR antagonists, but also to monitor response to EGFR antagonists [taking fine needle biopsies to provide tumor tissue during treatment]. Levels of CD82 above the 90th percentile suggest poorer efficacy from EGFR antagonists.

The tyrosine kinases abl, c-kit, PDGFRalpha, PDGFbeta, and ARG; also, the signal transmitting ligands c-kit ligand, PDGFA, B, C and D. The listed tyrosine kinases are all targets of the drug Gleevec™ (imatinib mesylate, Novartis), and the listed ligands stimulate one or more of the listed tyrosine kinases. In the two indications for which Gleevec™ is approved, tyrosine kinase targets (bcr-abl and ckit) are overexpressed and also contain activating mutations. A finding that one of the Gleevec™ target tyrosine kinase targets is expressed in breast cancer tissue

will prompt a second stage of analysis wherein the gene will be sequenced to determine whether it is mutated. That a mutation found is an activating mutation can be proved by methods known in the art, such as, for example, by measuring kinase enzyme activity or by measuring phosphorylation status of the particular kinase, relative to the corresponding wild-type kinase. Breast cancer patients whose tumors express high levels of mRNAs encoding Gleevec™ target tyrosine kinases, specifically, in the upper ten percentile, or mRNAs for Gleevec™ target tyrosine kinases in the average range and mRNAs for their cognate growth stimulating ligands in the upper ten percentile, are particularly good candidates for treatment with Gleevec™.

VEGF is a potent and pathologically important angiogenic factor. (See below under Prognostic Indicators.) When VEGF mRNA levels are in the upper ten percentile, aggressive treatment is warranted. Such levels particularly suggest the value of treatment with anti-angiogenic drugs, including VEGF antagonists, such as anti-VEGF antibodies. Additionally, KDR or CD31 mRNA level in the upper 20 percentile further increases likelihood of benefit from VEGF antagonists.

Farnesyl pyrophosphatase synthetase and geranyl geranyl pyrophosphatase synthetase. These enzymes are targets of commercialized bisphosphonate drugs, which were developed originally for treatment of osteoporosis but recently have begun to prescribe them off-label in breast cancer. Elevated levels of mRNAs encoding these enzymes in breast cancer tissue, above the 90th percentile, suggest use of bisphosphonates as a treatment option.

2. *Multidrug Resistance Factors*

These factors include 10 Genes: gamma glutamyl cysteine synthetase [GCS]; GST-α; GST-π; MDR-1; MRP1-4; breast cancer resistance protein [BCRP]; lung resistance protein [MVP]; SXR; YB-1.

GCS and both GST-α and GST-π regulate glutathione levels, which decrease cellular sensitivity to chemotherapeutic drugs and other toxins by reductive derivatization. Glutathione is a necessary cofactor for multi-drug resistant pumps, MDR-1 and the MRPs. MDR1 and MRPs function to actively transport out of cells several important chemotherapeutic drugs used in breast cancer.

GSTs, MDR-1, and MRP-1 have all been studied extensively to determine possible have prognostic or predictive significance in human cancer. However, a great deal of disagreement exists in the literature with respect to these questions. Recently, new members of the MRP family have been identified: MRP-2, MRP-3, MRP-4, BCRP, and lung resistance protein [major vault protein]. These have substrate specificities that overlap with those of MDR-1 and MRP-1. The incorporation of all of these relevant ABC family members as well as glutathione synthetic

enzymes into the present invention captures the contribution of this family to drug resistance, in a way that single or double analyte assays cannot.

MRP-1, the gene coding for the multidrug resistance protein.

P-glycoprotein, is not regulated primarily at the transcriptional level. However, p-glycoprotein stimulates the transcription of PTP1b. An embodiment of the present invention is the use of the level of the mRNA for the phosphatase PTP1b as a surrogate measure of MRP-1/p-glycoprotein activity.

The gene SXR is also an activator of multidrug resistance, as it stimulates transcription of certain multidrug resistance factors.

The impact of multidrug resistance factors with respect to chemotherapeutic agents used in breast cancer is as follows. Beneficial response to doxorubicin is compromised when the mRNA levels of either MDR1, GSTα, GSTπ, SXR, BCRP YB-1, or LRP/MVP are in the upper four percentile. Beneficial response to methotrexate is inhibited if mRNA levels of any of MRP1, MRP2, MRP3, or MRP4 or gamma-glutamyl cysteine synthetase are in the upper four percentile.

3. *__Eukaryotic Translation Initiation Factor 4E [EIF4E]__*

EIF4E mRNA levels provides evidence of protein expression and so expands the capability of RT-PCR to indicate variation in gene expression. Thus, one claim of the present invention is the use of EIF4E as an added indicator of gene expression of certain genes [e.g., cyclinD1, mdm2, VEGF, and others]. For example, in two tissue specimens containing the same amount of normalized VEGF mRNA, it is likely that the tissue containing the higher normalized level of EIF4E exhibits the greater level of VEGF gene expression.

The background is as follows. A key point in the regulation of mRNA translation is selection of mRNAs by the EIF4G complex to bind to the 43S ribosomal subunit. The protein EIF4E [the m7G CAP-binding protein] is often limiting because more mRNAs than EIF4E copies exist in cells. Highly structured 5'UTRs or highly GC-rich ones are inefficiently translated, and these often code for genes that carry out functions relevant to cancer [e.g., cyclinD1, mdm2, and VEGF]. EIF4E is itself regulated at the transcriptional/ mRNA level. Thus, expression of EIF4E provides added indication of increased activity of a number of proteins.

It is also noteworthy that overexpression of EIF4E transforms cultured cells, and hence is an oncogene. Overexpression of EIF4E occurs in several different types of carcinomas but is particularly significant in breast cancer. EIF4E is typically expressed at very low levels in normal breast tissue.

D. Prognostic Indicators

1. *DNA Repair Enzymes*

Loss of BRCA1 or BRCA2 activity via mutation represents the critical oncogenic step in the most common type[s] of familial breast cancer. The levels of mRNAs of these important enzymes are abnormal in subsets of sporadic breast cancer as well. Loss of signals from either [to within the lower ten percentile] heightens risk of short survival.

2. *Cell Cycle Regulators*

Cell cycle regulators include 14 genes: c-MYC; c-Src; Cyclin D1; Ha-Ras; mdm2; p14ARF; p21WAF1/CIP; p16INK4a/p14; p23; p27; p53; PI3K; PKC-epsilon; PKC-delta.

The gene for p53 [TP53] is mutated in a large fraction of breast cancers. Frequently p53 levels are elevated when loss of function mutation occurs. When the mutation is dominant-negative, it creates survival value for the cancer cell because growth is promoted and apoptosis is inhibited. Thousands of different p53 mutations have been found in human cancer, and the functional consequences of many of them are not clear. A large body of academic literature addresses the prognostic and predictive significance of mutated p53 and the results are highly conflicting. The present invention provides a functional genomic measure of p53 activity, as follows. The activated wild type p53 molecule triggers transcription of the cell cycle inhibitor p21. Thus, the ratio of p53 to p21 should be low when p53 is wild-type and activated. When p53 is detectable and the ratio of p53 to p21 is elevated in tumors relative to normal breast, it signifies nonfunctional or dominant negative p53. The cancer literature provides evidence for this as born out by poor prognosis.

Mdm2 is an important p53 regulator. Activated wildtype p53 stimulates transcription of mdm2. The mdm2 protein binds p53 and promotes its proteolytic destruction. Thus, abnormally low levels of mdm2 in the presence of normal or higher levels of p53 indicate that p53 is mutated and inactivated.

One aspect of the present invention is the use of ratios of mRNAs levels p53:p21 and p53:mdm2 to provide a picture of p53 status. Evidence for dominant negative mutation of p53 (as indicated by high p53:p21 and/or high p53:mdm2 mRNA ratios—specifically in the upper ten percentile) presages higher risk of recurrence in breast cancer and therefore weights toward a decision to use chemotherapy in node negative post surgery breast cancer.

Another important cell cycle regulator is p27, which in the activated form blocks cell cycle progression at the level of cdk4. The protein is regulated primarily via phosphorylation/dephosphorylation, rather than at the transcriptional level. However, levels of

p27 mRNAs do vary. Therefore a level of p27 mRNA in the upper ten percentile indicates reduced risk of recurrence of breast cancer post surgery.

Cyclin D1 is a principle positive regulator of entry into S phase of the cell cycle. The gene for cyclin D1 is amplified in about 20% of breast cancer patients, and therefore promotes tumor promotes tumor growth in those cases. One aspect of the present invention is use of cyclin D1 mRNA levels for diagnostic purposes in breast cancer. A level of cyclin D1 mRNA in the upper ten percentile suggests high risk of recurrence in breast cancer following surgery and suggests particular benefit of adjuvant chemotherapy.

3. *Other tumor suppressors and related proteins*

These include APC and E-cadherin. It has long been known that the tumor suppressor APC is lost in about 50% of colon cancers, with concomitant transcriptional upregulation of E-cadherin, an important cell adhesion molecule and growth suppressor. Recently, it has been found that the APC gene silenced in 15-40 % of breast cancers. Likewise, the E-cadherin gene is silenced [via CpG island methylation] in about 30% of breast cancers. An abnormally low level of APC and/or E-cadherin mRNA in the lower 5 percentile suggests high risk of recurrence in breast cancer following surgery and heightened risk of shortened survival.

4. *Regulators of Apoptosis*

These include BCl/BAX family members BCl2, Bcl-xl, Bak, Bax and related factors, NFκ-B and related factors, and also p53BP1/ASPP1 and p53BP2/ASPP2.

Bax and Bak are pro-apoptotic and BCl2 and Bcl-xl are anti-apoptotic. Therefore, the ratios of these factors influence the resistance or sensitivity of a cell to toxic (pro-apoptotic) drugs. In breast cancer, unlike other cancers, elevated level of BCl2 (in the upper ten percentile) correlates with good outcome. This reflects the fact that BCl2 has growth inhibitory activity as well as anti-apoptotic activity, and in breast cancer the significance of the former activity outweighs the significance of the latter. The impact of BCl2 is in turn dependent on the status of the growth stimulating transcription factor c-MYC. The gene for c-MYC is amplified in about 20% of breast cancers. When c-MYC message levels are abnormally elevated relative to BCl2 (such that this ratio is in the upper ten percentile), then elevated level of BCl2 mRNA is no longer a positive indicator.

NFκ-B is another important anti-apoptotic factor. Originally, recognized as a pro-inflammatory transcription factor, it is now clear that it prevents programmed cell death in response to several extracellular toxic factors [such as tumor necrosis factor]. The activity of this transcription factor is regulated principally via phosphorylation/dephosphorylation events. However, levels of NFκ-B nevertheless do vary from cell to cell, and elevated levels should

correlate with increased resistance to apoptosis. Importantly for present purposes, NFκ-B, exerts its anti-apoptotic activity largely through its stimulation of transcription of mRNAs encoding certain members of the IAP [inhibitor of apoptosis] family of proteins, specifically cIAP1, cIAP2, XIAP, and Survivin. Thus, abnormally elevated levels of mRNAs for these IAPs and for NFκ-B any in the upper 5 percentile] signify activation of the NFκ-B anti-apoptotic pathway. This suggests high risk of recurrence in breast cancer following chemotherapy and therefore poor prognosis. One embodiment of the present invention is the inclusion in the gene set of the above apoptotic regulators, and the above-outlined use of combinations and ratios of the levels of their mRNAs for prognosis in breast cancer.

The proteins p53BP1 and 2 bind to p53 and promote transcriptional activation of pro-apoptotic genes. The levels of p53BP1 and 2 are suppressed in a significant fraction of breast cancers, correlating with poor prognosis. When either is expressed in the lower tenth percentile poor prognosis is indicated.

5. *Factors that control cell invasion and angiogenesis*

These include uPA, PAI1, cathepsinsB, G and L, scatter factor [HGF], c-met, KDR, VEGF, and CD31. The plasminogen activator uPA and its serpin regulator PAI1 promote breakdown of extracellular matrices and tumor cell invasion. Abnormally elevated levels of both mRNAs in malignant breast tumors (in the upper twenty percentile) signify an increased risk of shortened survival, increased recurrence in breast cancer patients post surgery, and increased importance of receiving adjuvant chemotherapy. On the other hand, node negative patients whose tumors do not express elevated levels of these mRNA species are less likely to have recurrence of this cancer and could more seriously consider whether the benefits of standard chemotherapy justifies the associated toxicity.

Cathepsins B or L, when expressed in the upper ten percentile, predict poor disease-free and overall survival. In particular, cathepsin L predicts short survival in node positive patients.

Scatter factor and its cognate receptor c-met promote cell motility and invasion, cell growth, and angiogenesis. In breast cancer elevated levels of mRNAs encoding these factors should prompt aggressive treatment with chemotherapeutic drugs, when expression of either, or the combination, is above the 90^{th} percentile.

VEGF is a central positive regulator of angiogenesis, and elevated levels in solid tumors predict short survival [note many references showing that elevated level of VEGF predicts short survival]. Inhibitors of VEGF therefore slow the growth of solid tumors in animals and humans. VEGF activity is controlled at the level of transcription. VEGF mRNA levels in the upper ten percentile indicate significantly worse than average prognosis. Other markers of vascularization,

CD31 [PECAM], and KDR indicate high vessel density in tumors and that the tumor will be particularly malignant and aggressive, and hence that an aggressive therapeutic strategy is warranted.

6. *Markers for Immune and Inflammatory Cells and Processes*

These markers include the genes for Immunoglobulin light chain λ, CD18, CD3, CD68, Fas [CD95], and Fas Ligand.

Several lines of evidence suggest that the mechanisms of action of certain drugs used in breast cancer entail activation of the host immune/inflammatory response (For example, Herceptin®). One aspect of the present invention is the inclusion in the gene set of markers for inflammatory and immune cells, and markers that predict tumor resistance to immune surveillance. Immunoglobulin light chain lambda is a marker for immunoglobulin producing cells. CD18 is a marker for all white cells. CD3 is a marker for T-cells. CD68 is a marker for macrophages.

CD95 and Fas ligand are a receptor: ligand pair that mediate one of two major pathways by which cytotoxic T cells and NK cells kill targeted cells. Decreased expression of CD95 and increased expression of Fas Ligand indicates poor prognosis in breast cancer. Both CD95 and Fas Ligand are transmembrane proteins, and need to be membrane anchored to trigger cell death. Certain tumor cells produce a truncated soluble variant of CD95, created as a result of alternative splicing of the CD95 mRNA. This blocks NK cell and cytotoxic T cell Fas Ligand-mediated killing of the tumors cells. Presence of soluble CD95 correlates with poor survival in breast cancer. The gene set includes both soluble and full-length variants of CD95.

7. *Cell proliferation markers*

The gene set includes the cell proliferation markers Ki67/MiB1, PCNA, Pin1, and thymidine kinase. High levels of expression of proliferation markers associate with high histologic grade, and short survival. High levels of thymidine kinase in the upper ten percentile suggest in creased risk of short survival. Pin1 is a prolyl isomerase that stimulates cell growth, in part through the transcriptional activation of the cyclin D1 gene, and levels in the upper ten percentile contribute to a negative prognostic profile.

8. *Other growth factors and receptors*

This gene set includes IGF1, IGF2, IGFBP3, IGF1R, FGF2, FGFR1, CSF-1R/fms, CSF-1, IL6 and IL8. All of these proteins are expressed in breast cancer. Most stimulate tumor growth. However, expression of the growth factor FGF2 correlates with good outcome. Some have anti-apoptotic activity, prominently IGF1. Activation of the IGF1 axis via elevated IGF1, IGF1R, or

IGFBP3 (as indicated by the sum of these signals in the upper ten percentile) inhibits tumor cell death and strongly contributes to a poor prognostic profile.

9. *Gene expression markers that define subclasses of breast cancer*

These include: GRO1 oncogene alpha, Grb7, cytokeratins 5 and 17, retinal binding protein 4, hepatocyte nuclear factor 3, integrin alpha 7, and lipoprotein lipase. These markers subset breast cancer into different cell types that are phenotypically different at the level of gene expression. Tumors expressing signals for Bcl2, hepatocyte nuclear factor 3, LIV1 and ER above the mean have the best prognosis for disease free and overall survival following surgical removal of the cancer. Another category of breast cancer tumor type, characterized by elevated expression of lipoprotein lipase, retinol binding protein 4, and integrin α7, carry intermediate prognosis. Tumors expressing either elevated levels of cytokeratins 5, and 17, GRO oncogene at levels four-fold or greater above the mean, or ErbB2 and Grb7 at levels ten-fold or more above the mean, have worst prognosis.

Although throughout the present description, including the Examples below, various aspects of the invention are explained with reference to gene expression studies, the invention can be performed in a similar manner, and similar results can be reached by applying proteomics techniques that are well known in the art. The proteome is the totality of the proteins present in a sample (e.g. tissue, organism, or cell culture) at a certain point of time. Proteomics includes, among other things, study of the global changes of protein expression in a sample (also referred to as "expression proteomics"). Proteomics typically includes the following steps: (1) separation of individual proteins in a sample by 2-D gel electrophoresis (2-D PAGE); (2) identification of the individual proteins recovered from the gel, e.g. my mass spectrometry and/or N-terminal sequencing, and (3) analysis of the data using bioinformatics. Proteomics methods are valuable supplements to other methods of gene expression profiling, and can be used, alone or in combination with other methods of the present invention, to detect the products of the gene markers of the present invention.

Further details of the invention will be described in the following non-limiting Examples.

Example 1

Isolation of RNA from formalin-fixed, paraffin-embedded (FPET) tissue specimens

A. Protocols

I. EPICENTRE® Xylene Protocol

RNA Isolation

(1) Cut 1-6 sections (each 10 μm thick) of paraffin-embedded tissue per sample using a clean microtome blade and place into a 1.5 ml eppendorf tube.

(2) To extract paraffin, add 1 ml of xylene and invert the tubes for 10 minutes by rocking on a nutator.

(3) Pellet the sections by centrifugation for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(4) Remove the xylene, leaving some in the bottom to avoid dislodging the pellet.

(5) Repeat steps 2-4.

(6) Add 1 ml of 100% ethanol and invert for 3 minutes by rocking on the nutator.

(7) Pellet the debris by centrifugation for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(8) Remove the ethanol, leaving some at the bottom to avoid the pellet.

(9) Repeat steps 6-8 twice.

(10) Remove all of the remaining ethanol.

(11) For each sample, add 2 µl of 50 µg/µl Proteinase K to 300 µl of Tissue and Cell Lysis Solution.

(12) Add 300 µl of Tissue and Cell Lysis Solution containing the Proteinase K to each sample and mix thoroughly.

(13) Incubate at 65 °C for 90 minutes (vortex mixing every 5 minutes). Visually monitor the remaining tissue fragment. If still visible after 30 minutes, add an additional 2 µl of 50 µg/µl Proteinase K and continue incubating at 65 °C until fragment dissolves.

(14) Place the samples on ice for 3-5 minutes and proceed with protein removal and total nucleic acid precipitation.

Protein Removal and Precipitation of Total Nucleic Acid

(1) Add 150 µl of MPC Protein Precipitation Reagent to each lysed sample and vortex vigorously for 10 seconds.

(2) Pellet the debris by centrifugation for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(3) Transfer the supernatant into clean eppendorf tubes and discard the pellet.

(4) Add 500 µl of isopropanol to the recovered supernatant and thoroughly mix by rocking on the nutator for 3 minutes.

(5) Pellet the RNA/DNA by centrifugation at 4 °C for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(6) Remove all of the isopropanol with a pipet, being careful not to dislodge the pellet.

Removal of Contaminating DNA from RNA Preparations

(1) Prepare 200 µl of DNase I solution for each sample by adding 5 µl of RNase-Free DNase I (1 U/µl) to 195 µl of 1X DNase Buffer.

(2) Completely resuspend the pelleted RNA in 200 µl of DNase I solution by vortexing.

(3) Incubate the samples at 37 °C for 60 minutes.

(4) Add 200 µl of 2X T and C Lysis Solution to each sample and vortex for 5 seconds.

(5) Add 200 µl of MPC Protein Precipitation Reagent, mix by vortexing for 10 seconds and place on ice for 3-5 minutes.

(6) Pellet the debris by centrifugation for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(7) Transfer the supernatant containing the RNA to clean eppendorf tubes and discard the pellet. (Be careful to avoid transferring the pellet.)

(8) Add 500 µl of isopropanol to each supernatant and rock samples on the nutator for 3 minutes.

(9) Pellet the RNA by centrifugation at 4 °C for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(10) Remove the isopropanol, leaving some at the bottom to avoid dislodging the pellet.

(11) Rinse twice with 1 ml of 75% ethanol. Centrifuge briefly if the RNA pellet is dislodged.

(12) Remove ethanol carefully.

(13) Set under fume hood for about 3 minutes to remove residual ethanol.

(14) Resuspend the RNA in 30 µl of TE Buffer and store at -30 °C.

II. Hot Wax/Urea Protocol of the Invention

RNA Isolation

(1) Cut 3 sections (each 10 µm thick) of paraffin-embedded tissue using a clean microtome blade and place into a 1.5 ml eppendorf tube.

(2) Add 300 µl of lysis buffer (10 mM Tris 7.5, 0.5% sodium lauroyl sarcosine, 0.1 mM EDTA pH 7.5, 4M Urea) containing 330 µg/ml Proteinase K (added freshly from a 50 µg/µl stock solution) and vortex briefly.

(3) Incubate at 65 °C for 90 minutes (vortex mixing every 5 minutes). Visually monitor the tissue fragment. If still visible after 30 minutes, add an additional 2 µl of 50 µg/µl Proteinase K and continue incubating at 65 °C until fragment dissolves.

(4) Centrifuge for 5 minutes at 14,000 x g and transfer upper aqueous phase to new tube, being careful not to disrupt the paraffin seal.

(5) Place the samples on ice for 3-5 minutes and proceed with protein removal and total nucleic acid precipitation.

Protein Removal and Precipitation of Total Nucleic Acid

(1) Add 150 µl of 7.5M NH_4OAc to each lysed sample and vortex vigorously for 10 seconds.

(2) Pellet the debris by centrifugation for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(3) Transfer the supernatant into clean eppendorf tubes and discard the pellet.

(4) Add 500 µl of isopropanol to the recovered supernatant and thoroughly mix by rocking on the nutator for 3 minutes.

(5) Pellet the RNA/DNA by centrifugation at 4 °C for 10 minutes at 14,000 x g in an eppendorf microcentrifuge.

(6) Remove all of the isopropanol with a pipet, being careful not to dislodge the pellet.

Removal of Contaminating DNA from RNA Preparations

(1) Add 45 µl of 1X DNase I buffer (10 mM Tris-Cl, pH 7,5, 2.5 mM $MgCl_2$, 0.1 mM $CaCl_2$) and 5 µl of RNase-Free DNase I (2U/µl, Ambion) to each sample.

(2) Incubate the samples at 37 °C for 60 minutes.

Inactivate the DNaseI by heating at 70 °C for 5 minutes.

B. Results

Experimental evidence demonstrates that the hot RNA extraction protocol of the invention does not compromise RNA yield. Using 19 FPE breast cancer specimens, extracting RNA from three adjacent sections in the same specimens, RNA yields were measured via capillary electrophoresis with fluorescence detection (Agilent Bioanalyzer). Average RNA yields in nanograms and standard deviations with the invented and commercial methods, respectively, were: 139+/-21 versus 141+/-34.

Also, it was found that the urea-containing lysis buffer of the present invention can be substituted for the EPICENTRE® T&C lysis buffer, and the 7.5 M NH_4OAc reagent used for protein precipitation in accordance with the present invention can be substituted for the

EPICENTRE® MPC protein precipitation solution with neither significant compromise of RNA yield nor TaqMan® efficiency.

Example 2

Amplification of mRNA Species Prior to RT-PCR

The method described in section 10 above was used with RNA isolated from fixed, paraffin-embedded breast cancer tissue. TaqMan® analyses were performed with first strand cDNA generated with the T7-GSP primer (unamplified (T7-GSPr)), T7 amplified RNA (amplified (T7-GSPr)). RNA was amplified according to step 2 of Figure 4. As a control, TaqMan® was also performed with cDNA generated with an unmodified GSPr (amplified (GSPr)). An equivalent amount of initial template (1 ng/well) was used in each TaqMan® reaction.

The results are shown in Figure 8. *In vitro* transcription increased RT-PCR signal intensity by more than 10 fold, and for certain genes by more than 100 fold relative to controls in which the RT-PCR primers were the same primers used in method 2 for the generation of double-stranded DNA for *in vitro* transcription (GSP-$T7_r$ and GSP_f). Also shown in Figure 8 are RT-PCR data generated when standard optimized RT-PCR primers (i.e., lacking T7 tails) were used. As shown, compared to this control, the new method yielded substantial increases in RT-PCR signal (from 4 to 64 fold in this experiment).

The new method requires that each T7-GSP sequence be optimized so that the increase in the RT-PCR signal is the same for each gene, relative to the standard optimized RT-PCR (with non-T7 tailed primers).

Example 3

A Study of Gene Expression in Premalignant and Malignant Breast Tumors

A gene expression study was designed and conducted with the primary goal to molecularly characterize gene expression in paraffin-embedded, fixed tissue samples of invasive breast ductal carcinoma, and to explore the correlation between such molecular profiles and disease-free survival. A further objective of the study was to compare the molecular profiles in tissue samples of invasive breast cancer with the molecular profiles obtained in ductal carcinoma *in situ*. The study was further designed to obtain data on the molecular profiles in lobular carcinoma *in situ* and in paraffin-embedded, fixed tissue samples of invasive lobular carcinoma.

Molecular assays were performed on paraffin-embedded, formalin-fixed primary breast tumor tissues obtained from 202 individual patients diagnosed with breast cancer. All patients underwent surgery with diagnosis of invasive ductal carcinoma of the breast, pure ductal carcinoma in situ (DCIS), lobular carcinoma of the breast, or pure lobular carcinoma in situ

(LCIS). Patients were included in the study only if histopathologic assessment, performed as described in the Materials and Methods section, indicated adequate amounts of tumor tissue and homogeneous pathology.

The individuals participating in the study were divided into the following groups:

Group 1: Pure ductal carcinoma in situ (DCIS); n=18

Group 2: Invasive ductal carcinoma n=130

Group 3: Pure lobular carcinoma in situ (LCIS); n=7

Group 4: Invasive lobular carcinoma n=16

Materials and Methods

Each representative tumor block was characterized by standard histopathology for diagnosis, semi-quantitative assessment of amount of tumor, and tumor grade. A total of 6 sections (10 microns in thickness each) were prepared and placed in two Costar Brand Microcentrifuge Tubes (Polypropylene, 1.7 mL tubes, clear; 3 sections in each tube). If the tumor constituted less than 30% of the total specimen area, the sample may have been crudely dissected by the pathologist, using gross microdissection, putting the tumor tissue directly into the Costar tube.

If more than one tumor block was obtained as part of the surgical procedure, all tumor blocks were subjected to the same characterization, as described above, and the block most representative of the pathology was used for analysis.

Gene Expression Analysis

mRNA was extracted and purified from fixed, paraffin-embedded tissue samples, and prepared for gene expression analysis as described in chapters 7-11 above.

Molecular assays of quantitative gene expression were performed by RT-PCR, using the ABI PRISM 7900™ Sequence Detection System™ (Perkin-Elmer-Applied Biosystems, Foster City, CA, USA). ABI PRISM 7900™ consists of a thermocycler, laser, charge-coupled device (CCD), camera and computer. The system amplifies samples in a 384-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 384 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

Analysis and Results

Tumor tissue was analyzed for 185 cancer-related genes and 7 reference genes. The threshold cycle (CT) values for each patient were normalized based on the median of all genes

for that particular patient. Clinical outcome data were available for all patients from a review of registry data and selected patient charts.

Outcomes were classified as:

0 died due to breast cancer or to unknown cause or alive with breast cancer recurrence;

1 alive without breast cancer recurrence or died due to a cause other than breast cancer

Analysis was performed by:

1. Analysis of the relationship between normalized gene expression and the binary outcomes of 0 or 1.

2. Analysis of the relationship between normalized gene expression and the time to outcome (0 or 1 as defined above) where patients who were alive without breast cancer recurrence or who died due to a cause other than breast cancer were censored. This approach was used to evaluate the prognostic impact of individual genes and also sets of multiple genes.

Analysis of 147 patients with invasive breast carcinoma by binary approach

In the first (binary) approach, analysis was performed on all 146 patients with invasive breast carcinoma. A t test was performed on the group of patients classified as 0 or 1 and the p-values for the differences between the groups for each gene were calculated.

The following Table 4 lists the 45 genes for which the p-value for the differences between the groups was <0.05.

Table 4

Gene/ SEQ ID NO:	Mean CT Alive	Mean CT Deceased	t-value	Degrees of freedom	p
FOXM1	33.66	32.52	3.92	144	0.0001
PRAME	35.45	33.84	3.71	144	0.0003
Bcl2	28.52	29.32	-3.53	144	0.0006
STK15	30.82	30.10	3.49	144	0.0006
CEGP1	29.12	30.86	-3.39	144	0.0009
Ki-67	30.57	29.62	3.34	144	0.0011
GSTM1	30.62	31.63	-3.27	144	0.0014
CA9	34.96	33.54	3.18	144	0.0018
PR	29.56	31.22	-3.16	144	0.0019
BBC3	31.54	32.10	-3.10	144	0.0023
NME1	27.31	26.68	3.04	144	0.0028
SURV	31.64	30.68	2.92	144	0.0041
GATA3	26.06	26.99	-2.91	144	0.0042
TFRC	28.96	28.48	2.87	144	0.0047
YB-1	26.72	26.41	2.79	144	0.0060
DPYD	28.51	28.84	-2.67	144	0.0084
GSTM3	28.21	29.03	-2.63	144	0.0095
RPS6KB1	31.18	30.61	2.61	144	0.0099
Src	27.97	27.69	2.59	144	0.0105
Chk1	32.63	31.99	2.57	144	0.0113
ID1	28.73	29.13	-2.48	144	0.0141
EstR1	24.22	25.40	-2.44	144	0.0160
p27	27.15	27.51	-2.41	144	0.0174
CCNB1	31.63	30.87	2.40	144	0.0176
XIAP	30.27	30.51	-2.40	144	0.0178
Chk2	31.48	31.11	2.39	144	0.0179
CDC25B	29.75	29.39	2.37	144	0.0193
IGF1R	28.85	29.44	-2.34	144	0.0209

AK055699	33.23	34.11	-2.28	144	0.0242
PI3KC2A	31.07	31.42	-2.25	144	0.0257
TGFB3	28.42	28.85	-2.25	144	0.0258
BAGI1	28.40	28.75	-2.24	144	0.0269
CYP3A4	35.70	35.32	2.17	144	0.0317
EpCAM	28.73	28.34	2.16	144	0.0321
VEGFC	32.28	31.82	2.16	144	0.0326
pS2	28.96	30.60	-2.14	144	0.0341
hENT1	27.19	26.91	2.12	144	0.0357
WISP1	31.20	31.64	-2.10	144	0.0377
HNF3A	27.89	28.64	-2.09	144	0.0384
NFKBp65	33.22	33.80	-2.08	144	0.0396
BRCA2	33.06	32.62	2.08	144	0.0397
EGFR	30.68	30.13	2.06	144	0.0414
TK1	32.27	31.72	2.02	144	0.0453
VDR	30.08	29.73	1.99	144	0.0488

In the foregoing Table 4, lower (negative) t-values indicate higher expression (or lower CTs), associated with better outcomes, and, inversely, higher (positive) t-values indicate higher expression (lower CTs) associated with worse outcomes. Thus, for example, elevated expression of the FOXM1 gene (t-value = 3.92, CT mean alive> CT mean deceased) indicates a reduced likelihood of disease free survival. Similarly, elevated expression of the CEGP1 gene (t-value = -3.39; CT mean alive< CT mean deceased) indicates an increased likelihood of disease free survival.

Based on the data set forth in Table 4, the overexpression of any of the following genes in breast cancer indicates a reduced likelihood of survival without cancer recurrence following surgery: FOXM1; PRAME; SKT15, Ki-67; CA9; NME1; SURV; TFRC; YB-1; RPS6KB1; Src; Chk1; CCNB1; Chk2; CDC25B; CYP3A4; EpCAM; VEGFC; hENT1; BRCA2; EGFR; TK1; VDR.

Based on the data set forth in Table 4, the overexpression of any of the following genes in breast cancer indicates a better prognosis for survival without cancer recurrence following surgery: Blc12; CEGP1; GSTM1; PR; BBC3; GATA3; DPYD; GSTM3; ID1; EstR1; p27; XIAP; IGF1R; AK055699; P13KC2A; TGFB3; BAGI1; pS2; WISP1; HNF3A; NFKBp65.

Analysis of 108 ER positive patient by binary approach

108 patients with normalized CT for estrogen receptor (ER) < 25.2 (i.e., ER positive patients) were subjected to separate analysis. A t test was performed on the groups of patients classified as 0 or 1 and the p-values for the differences between the groups for each gene were calculated. The following Table 5 lists the 12 genes where the p-value for the differences between the groups was <0.05.

Table 5

Gene/ SEQ ID NO:	Mean CT Alive	Mean CT Deceased	t-value	Degrees of freedom	p
PRAME	35.54	33.88	3.03	106	0.0031
Bcl2	28.24	28.87	-2.70	106	0.0082
FOXM1	33.82	32.85	2.66	106	0.089
DIABLO	30.33	30.71	-2.47	106	0.0153
EPHX1	28.62	28.03	2.44	106	0.0163
HIF1A	29.37	28.88	2.40	106	0.0180
VEGFC	32.39	31.69	2.39	106	0.0187
Ki-67	30.73	29.82	2.38	106	0.0191
IGF1R	28.60	29.18	-2.37	106	0.0194
VDR	30.14	29.60	2.17	106	0.0322
NME1	27.34	26.80	2.03	106	0.0452
GSTM3	28.08	28.92	-2.00	106	0.0485

For each gene, a classification algorithm was utilized to identify the best threshold value (CT) for using each gene alone in predicting clinical outcome.

Based on the data set forth in Table 5, overexpression of the following genes in ER-positive cancer is indicative of a reduced likelihood of survival without cancer recurrence following surgery: PRAME; FOXM1; EPHX1; HIF1A; VEGFC; Ki-67; VDR; NME1. Some of these genes (PRAME; FOXM1; VEGFC; Ki-67; VDR; and NME1) were also identified as indicators of poor prognosis in the previous analysis, not limited to ER-positive breast cancer. The overexpression of the remaining genes (EPHX1 and HIF1A) appears to be negative indicator of disease free survival in ER-positive breast cancer only. Based on the data set forth in Table 5, overexpression of the following genes in ER-positive cancer is indicative of a better

prognosis for survival without cancer recurrence following surgery: Bcl-2; DIABLO; IGF1R; GSTM3. Of the latter genes, Bcl-2; IGFR1; and GSTM3 have also been identified as indicators of good prognosis in the previous analysis, not limited to ER-positive breast cancer. The overexpression of DIABLO appears to be positive indicator of disease free survival in ER-positive breast cancer only.

Analysis of multiple genes and indicators of outcome

Two approaches were taken in order to determine whether using multiple genes would provide better discrimination between outcomes.

First, a discrimination analysis was performed using a forward stepwise approach. Models were generated that classified outcome with greater discrimination than was obtained with any single gene alone.

According to a second approach (time-to-event approach), for each gene a Cox Proportional Hazards model (see, e.g. Cox, D. R., and Oakes, D. (1984), *Analysis of Survival Data*, Chapman and Hall, London, New York) was defined with time to recurrence or death as the dependent variable, and the expression level of the gene as the independent variable. The genes that have a p-value < 0.05 in the Cox model were identified. For each gene, the Cox model provides the relative risk (RR) of recurrence or death for a unit change in the expression of the gene. One can choose to partition the patients into subgroups at any threshold value of the measured expression (on the CT scale), where all patients with expression values above the threshold have higher risk, and all patients with expression values below the threshold have lower risk, or vice versa, depending on whether the gene is an indicator of good (RR>1.01) or poor (RR<1.01) prognosis. Thus, any threshold value will define subgroups of patients with respectively increased or decreased risk. The results are summarized in the following Tables 6 and 7.

Table 6

Cox Model Results for 146 Patients with Invasive Breast Cancer

Gene	Relative Risk (RR)	SE Relative Risk	p value
FOXM1	0.58	0.15	0.0002
STK15	0.51	0.20	0.0006
PRAME	0.78	0.07	0.0007
Bcl2	1.66	0.15	0.0009
CEGP1	1.25	0.07	0.0014
GSTM1	1.40	0.11	0.0014
Ki67	0.62	0.15	0.0016
PR	1.23	0.07	0.0017
Contig51037	0.81	0.07	0.0022
NME1	0.64	0.15	0.0023
YB-1	0.39	0.32	0.0033
TFRC	0.53	0.21	0.0035
BBC3	1.72	0.19	0.0036
GATA3	1.32	0.10	0.0039
CA9	0.81	0.07	0.0049
SURV	0.69	0.13	0.0049
DPYD	2.58	0.34	0.0052
RPS6KB1	0.60	0.18	0.0055
GSTM3	1.36	0.12	0.0078
Src.2	0.39	0.36	0.0094
TGFB3	1.61	0.19	0.0109
CDC25B	0.54	0.25	0.0122
XIAP	3.20	0.47	0.0126
CCNB1	0.68	0.16	0.0151
IGF1R	1.42	0.15	0.0153
Chk1	0.68	0.16	0.0155
ID1	1.80	0.25	0.0164
p27	1.69	0.22	0.0168
Chk2	0.52	0.27	0.0175

EstR1	1.17	0.07	0.0196
HNF3A	1.21	0.08	0.206
pS2	1.12	0.05	0.0230
BAGI1	1.88	0.29	0.0266
AK055699	1.24	0.10	0.0276
pENT1	0.51	0.31	0.0293
EpCAM	0.62	0.22	0.0310
WISP1	1.39	0.16	0.0338
VEGFC	0.62	0.23	0.0364
TK1	0.73	0.15	0.0382
NFKBp65	1.32	0.14	0.0384
BRCA2	0.66	0.20	0.0404
CYP3A4	0.60	0.25	0.0417
EGFR	0.72	0.16	0.0436

Table 7

Cox Model Results for 108 Patients wih ER+ Invasive Breast Cancer

Gene	Relative Risk (RR)	SE Relative Risk	p-value
PRAME	0.75	0.10	0.0045
Contig51037	0.75	0.11	0.0060
Blc2	2.11	0.28	0.0075
HIF1A	0.42	0.34	0.0117
IGF1R	1.92	0.26	0.0117
FOXM1	0.54	0.24	0.0119
EPHX1	0.43	0.33	0.0120
Ki67	0.60	0.21	0.0160
CDC25B	0.41	0.38	0.0200
VEGFC	0.45	0.37	0.0288
CTSB	0.32	0.53	0.0328
DIABLO	2.91	0.50	0.0328
p27	1.83	0.28	0.0341
CDH1	0.57	0.27	0.0352
IGFBP3	0.45	0.40	0.0499

The binary and time-to-event analyses, with few exceptions, identified the same genes as prognostic markers. For example, comparison of Tables 4 and 6 shows that, with the exception of a single gene, the two analyses generated the same list of top 15 markers (as defined by the smallest p values). Furthermore, when both analyses identified the same gene, they were concordant with respect to the direction (positive or negative sign) of the correlation with survival/recurrence. Overall, these results strengthen the conclusion that the identified markers have significant prognostic value.

For Cox models comprising more than two genes (multivariate models), stepwise entry of each individual gene into the model is performed, where the first gene entered is pre-selected from among those genes having significant univariate p-values, and the gene selected for entry into the model at each subsequent step is the gene that best improves the fit of the model to the data. This analysis can be performed with any total number of genes. In the analysis the results of which are shown below, stepwise entry was performed for up to 10 genes.

Multivariate analysis is performed using the following equation:

RR=exp[coef(geneA) x Ct(geneA) + coef(geneB) x Ct(geneB) + coef(geneC) x Ct(geneC) + ...].

In this equation, coefficiencts for genes that are predictors of beneficial outcome are positive numbers and coefficients for genes that are predictors of unfavorable outcome are negative numbers. The "Ct" values in the equation are ΔCts, i.e. reflect the difference between the average normalized Ct value for a population and the normalized Ct measured for the patient in question. The convention used in the present analysis has been that ΔCts below and above the population average have positive signs and negative signs, respectively (reflecting greater or lesser mRNA abundance). The relative risk (RR) calculated by solving this equation will indicate if the patient has an enhanced or reduced chance of long-term survival without cancer recurrence.

Multivariate gene analysis of 147 patients with invasive breast carcinoma

(a) A multivariate stepwise analysis, using the Cox Proportional Hazards Model, was performed on the gene expression data obtained for all 147 patients with invasive breast carcinoma. Genes CEGP1, FOXM1, STK15 and PRAME were excluded from this analysis. The following ten-gene sets have been identified by this analysis as having particularly strong predictive value of patient survival without cancer recurrence following surgical removal of primary tumor.

1. Bcl2, cyclinG1, NFKBp65, NME1, EPHX1, TOP2B, DR5, TERC, Src, DIABLO;

2. Ki67, XIAP, hENT1, TS, CD9, p27, cyclinG1, pS2, NFKBp65, CYP3A4;

3. GSTM1, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, NFKBp65, ErbB3;

4. PR, NME1, XIAP, upa, cyclinG1, Contig51037, TERC, EPHX1, ALDH1A3, CTSL;

5. CA9, NME1, TERC, cyclinG1, EPHX1, DPYD, Src, TOP2B, NFKBp65, VEGFC;

6. TFRC, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, ErbB3, NFKBp65.

(b) A multivariate stepwise analysis, using the Cox Proportional Hazards Model, was performed on the gene expression data obtained for all 147 patients with invasive breast carcinoma, using an interrogation set including a reduced number of genes. The following ten-gene sets have been identified by this analysis as having particularly strong predictive value of patient survival without cancer recurrence following surgical removal of primary tumor.

1. Bcl2, PRAME, cyclinG1, FOXM1, NFKBp65, TS, XIAP, Ki67, CYP3A4, p27;

2. FOXM1, cyclinG1, XIAP, Contig51037, PRAME, TS, Ki67, PDGFRa, p27, NFKBp65;

3. PRAME, FOXM1, cyclinG1, XIAP, Contig51037, TS, Ki6, PDGFRa, p27, NFKBp65;

4. Ki67, XIAP, PRAME, hENT1, contig51037, TS, CD9, p27, ErbB3, cyclinG1;

5. STK15, XIAP, PRAME, PLAUR, p27, CTSL, CD18, PREP, p53, RPS6KB1;

6. GSTM1, XIAP, PRAME, p27, Contig51037, ErbB3, GSTp, EREG, ID1, PLAUR;

7. PR, PRAME, NME1, XIAP, PLAUR, cyclinG1, Contig51037, TERC, EPHX1, DR5;

8. CA9, FOXM1, cyclinG1, XIAP, TS, Ki67, NFKBp65, CYP3A4, GSTM3, p27;

9. TFRC, XIAP, PRAME, p27, Contig51037, ErbB3, DPYD, TERC, NME1, VEGFC;

10. CEGP1, PRAME, hENT1, XIAP, Contig51037, ErbB3, DPYD, NFKBp65, ID1, TS.

Multivariate analysis of patients with ER positive invasive breast carcinoma

A multivariate stepwise analysis, using the Cox Proportional Hazards Model, was performed on the gene expression data obtained for patients with ER positive invasive breast carcinoma. The following ten-gene sets have been identified by this analysis as having particularly strong predictive value of patient survival without cancer recurrence following surgical removal of primary tumor.

1. PRAME, p27, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;
2. Contig51037, EPHX1, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;
3. Bcl2, hENT1, FOXM1, Contig51037, cyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;
4. HIF1A, PRAME, p27, IGFBP2, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;
5. IGF1R, PRAME, EPHX1, Contig51037, cyclinG1, Bcl2, NME1, PTEN, TBP, TIMP2;
6. FOXM1, Contig51037, VEGFC, TBP, HIF1A, DPYD, RAD51C, DCR3, cyclinG1, BAG1;
7. EPHX1, Contig51037, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;
8. Ki67, VEGFC, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;
9. CDC25B, Contig51037, hENT1, Bcl2, HLAG, TERC, NME1, upa, ID1, CYP;
10. VEGFC, Ki67, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;
11. CTSB, PRAME, p27, IGFBP2, EPHX1, CTSL, BAD, DR5, DCR3, XIAP;
12. DIABLO, Ki67, hENT1, TIMP2, ID1, p27, KRT19, IGFBP2, TS, PDGFB;
13. p27, PRAME, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;
14. CDH1; PRAME, VEGFC; HIF1A; DPYD, TIMP2, CYP3A4, EstR1, RBP4, p27;
15. IGFBP3, PRAME, p27, Bcl2, XIAP, EstR1, Ki67, TS, Src, VEGF;
16. GSTM3, PRAME, p27, IGFBP3, XIAP, FGF2, hENT1, PTEN, EstR1, APC;
17. hENT1, Bcl2, FOXM1, Contig51037, CyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;
18. STK15, VEGFC, PRAME, p27, GCLC, hENT1, ID1, TIMP2, EstR1, MCP1;

19. NME1, PRAM, p27, IGFBP3, XIAP, PTEN, hENT1, Bcl2, CYP3A4, HLAG;
20. VDR, Bcl2, p27, hENT1, p53, PI3KC2A, EIF4E, TFRC, MCM3, ID1;
21. EIF4E, Contig51037, EPHX1, cyclinG1, Bcl2, DR5, TBP, PTEN, NME1, HER2;
22. CCNB1, PRAME, VEGFC, HIF1A, hENT1, GCLC, TIMP2, ID1, p27, upa;
23. ID1, PRAME, DIABLO, hENT1, p27, PDGFRa, NME1, BIN1, BRCA1, TP;
24. FBXO5, PRAME, IGFBP3, p27, GSTM3, hENT1, XIAP, FGF2, TS, PTEN;
25. GUS, HIA1A, VEGFC, GSTM3, DPYD, hENT1, FBXO5, CA9, CYP, KRT18;
26. Bclx, Bcl2, hENT1, Contig51037, HLAG, CD9, ID1, BRCA1, BIN1, HBEGF.

It is noteworthy that many of the foregoing gene sets include genes that alone did not have sufficient predictive value to qualify as prognostic markers under the standards discussed above, but in combination with other genes, their presence provides valuable information about the likelihood of long-term patient survival without cancer recurrence

All references cited throughout the disclosure are hereby expressly incorporated by reference.

While the present invention has been described with reference to what are considered to be the specific embodiments, it is to be understood that the invention is not limited to such embodiments. To the contrary, the invention is intended to cover various modifications and equivalents included within the spirit and scope of the appended claims. For example, while the disclosure focuses on the identification of various breast cancer associated genes and gene sets, and on the diagnosis and treatment of breast cancer, similar genes, gene sets and methods concerning other types of cancer are specifically within the scope herein.

WHAT IS CLAIMED IS:

1. A method for predicting clinical outcome for a patient diagnosed with cancer, comprising

determining the expression level of one or more genes, or their expression products, selected from the group consisting of p53BP2, cathepsin B, cathepsin L, Ki67/MiB1, and thymidine kinase in a cancer tissue obtained from the patient, normalized against a control gene or genes, and compared to the amount found in a reference cancer tissue set,

wherein a poor outcome is predicted if:

(a) the expression level of p53BP2 is in the lower 10^{th} percentile; or

(b) the expression level of either cathepsin B or cathepsin L is in the upper 10^{th} percentile; or

(c) the expression level of any either Ki67/MiB1 or thymidine kinase is in the upper 10^{th} percentile.

2. The method of claim 1 wherein poor clinical outcome is measured in terms of shortened survival or increased risk of cancer recurrence.

3. The method of claim 2 wherein poor clinical outcome is measured in terms of shortened survival or increased risk of cancer recurrence following surgical removal of the cancer.

4. The method of claim 1 wherein the cancer is selected from the group consisting of breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer.

5. The method of claim 4 wherein the cancer is breast cancer.

6. The method of claim 5 wherein the expression level of p53BP2 is determined.

7. The method of claim 5 wherein the expression levels of cathepsin B and cathepsin L are determined.

8. The method of claim 5 wherein the expression level of cathepsin L is determined.

9. The method of claim 5 wherein the expression levels of Ki67/MiB1 and thymidine kinase are determined.

10. The method of claim 5 wherein the expression level of Ki67/MiB1 is determined.

11. The method of claim 5 wherein the expression level of thymidine kinase is determined.

12. The method of claim 1 wherein the expression level of more than one gene, or gene product, is determined.

13. The method of claim 1 wherein the expression level of more than two genes is determined.

14. The method of claim 13 further comprising the step of subjecting the expression data to multivariate analysis using the Cox Proportional Hazards model.

15. The method of claim 1 wherein the expression level is determined using RNA obtained from a formalin-fixed, paraffin-embedded tissue sample.

16. The method of claim 1 wherein the expression level is determined by reverse phase polymerase chain reaction (RT-PCR).

17. The method of claim 16 wherein said RNA is fragmented.

18. A method of predicting the likelihood of the recurrence of cancer following treatment in a cancer patient, comprising determining the expression level of p27, or its expression product, in a cancer tissue obtained from said patient, normalized against a control gene or genes, and compared to the amount found in a reference cancer tissue set, wherein an expression level in the upper 10th percentile indicates decreased risk of recurrence following treatment.

19. The method of claim 18 wherein the cancer is selected from the group consisting of breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer,

pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer.

20. The method of claim 19 wherein the cancer is breast cancer.

21. The method of claim 20 wherein the expression level is determined following surgical removal of cancer.

22. The method of claim 20 wherein the expression level is determined using RNA obtained from a formalin-fixed, paraffin-embedded tissue sample.

23. The method of claim 22 wherein said RNA is fragmented.

24. The method of claim 22 wherein the expression level is determined by reverse phase polymerase chain reaction (RT-PCR).

25. A method for classifying cancer comprising, determining the expression level of two or more genes selected from the group consisting of Bcl2, hepatocyte nuclear factor 3, ER, ErbB2 and Grb7, or their expression products, in a cancer tissue, normalized against a control gene or genes, and compared to the amount found in a reference cancer tissue set, wherein (i) tumors expressing at least one of Bcl2, hepatocyte nuclear factor 3, and ER, or their expression products, above the mean expression level in the reference tissue set are classified as having a good prognosis for disease free and overall patient survival following treatment; and (ii) tumors expressing elevated levels of ErbB2 and Grb7, or their expression products, at levels ten-fold or more above the mean expression level in the reference tissue set are classified as having poor prognosis of disease free and overall patient survival following treatment.

26. The method of claim 26 wherein the cancer is selected from the group consisting of breast cancer, colon cancer, lung cancer, prostate cancer, hepatocellular cancer, gastric cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, cancer of the urinary tract, thyroid cancer, renal cancer, carcinoma, melanoma, and brain cancer.

27. The method of claim 26 wherein the cancer is breast cancer.

28. The method of claim 26 wherein the expression level is determined following surgical removal of cancer.

29. The method of claim 26 wherein the expression level is determined using RNA obtained from a formalin-fixed, paraffin-embedded tissue sample.

30. The method of claim 29 wherein said RNA is fragmented.

31. The method of claim 29 wherein the expression level is determined by reverse phase polymerase chain reaction (RT-PCR).

32. A method of predicting the likelihood of long-term survival of a breast cancer patient without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising determining the expression level of one or more prognostic RNA transcripts or their product in a breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products, wherein the prognostic transcript is the transcript of one or more genes selected from the group consisting of: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, CA9, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, GSTM3, RPS6KB1, Src, Chk1, ID1, EstR1, p27, CCNB1, XIAP, Chk2, CDC25B, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, CYP3A4, EpCAM, VEGFC, pS2, hENT1, WISP1, HNF3A, NFKBp65, BRCA2, EGFR, TK1, VDR, Contig51037, pENT1, EPHX1, IF1A, DIABLO, CDH1, HIF1α, IGFBP3, CTSB, and Her2, wherein overexpression of one or more of FOXM1, PRAME, STK15, Ki-67, CA9, NME1, SURV, TFRC, YB-1, RPS6KB1, Src, Chk1, CCNB1, Chk2, CDC25B, CYP3A4, EpCAM, VEGFC, hENT1, BRCA2, EGFR, TK1, VDR, EPHX1, IF1A, Contig51037, CDH1, HIF1α, IGFBP3, CTSB, Her2, and pENT1 indicates a decreased likelihood of long-term survival without breast cancer recurrence, and the overexpression of one or more of Bcl2, CEGP1, GSTM1, PR, BBC3, GATA3, DPYD, GSTM3, ID1, EstR1, p27, XIAP, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, pS2, WISP1, HNF3A, NFKBp65, and DIABLO indicates an increased likelihood of long-term survival without breast cancer recurrence.

33. The method of claim 32 comprising determining the expression level of at least two of said prognostic transcipts or their expression products.

34. The method of claim 32 wherein the breast cancer is invasive breast carcinoma, comprising determination of the expression levels of the transcripts of the following genes, or their expression products: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, CA9, Contig51037, RPS6K1 and Her2.

35. The method of claim 32 wherein said breast cancer is characterized by overexpression of the estrogen receptor (ER).

36. The method of claim 35 comprising determination of the expression levels of the transcripts of at least two of the following genes, or their expression products: PRAME, Bcl2, FOXM1, DIABLO, EPHX1, HIF1A, VEGFC, Ki-67, IGF1R, VDR, NME1, GSTM3, Contig51037, CDC25B, CTSB, p27, CDH1, and IGFBP3.

37. The method of claim 32 wherein the expression level of one or more prognostic RNA transcripts is determined.

38. The method of claim 37 wherein said RNA is isolated from a fixed, wax-embedded breast cancer tissue specimen of said patient.

39. An array comprising polynucleotides hybridizing to the following genes: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, CA9, Contig51037, RPS6K1 and Her2, immobilized on a solid surface.

40. The array of claim 39 comprising polynucleotides hybridizing to the following genes: FOXM1, PRAME, Bcl2, STK15, CEGP1, Ki-67, GSTM1, CA9, PR, BBC3, NME1, SURV, GATA3, TFRC, YB-1, DPYD, GSTM3, RPS6KB1, Src, Chk1, ID1, EstR1, p27, CCNB1, XIAP, Chk2, CDC25B, IGF1R, AK055699, P13KC2A, TGFB3, BAGI1, CYP3A4, EpCAM, VEGFC, pS2, hENT1, WISP1, HNF3A, NFKBp65, BRCA2, EGFR, TK1, VDR, Contig51037, pENT1, EPHX1, IF1A, CDH1, HIF1α, IGFBP3, CTSB, Her2 and DIABLO, immobilized on a solid surface.

41. A method of predicting the likelihood of long-term survival of a patient diagnosed with invasive breast cancer, without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising the steps of:

(1) determining the expression levels of the RNA transcripts or the expression products of genes of a gene set selected from the group consisting of

(a) Bcl2, cyclinG1, NFKBp65, NME1, EPHX1, TOP2B, DR5, TERC, Src, DIABLO;

(b) Ki67, XIAP, hENT1, TS, CD9, p27, cyclinG1, pS2, NFKBp65, CYP3A4;

(c) GSTM1, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, NFKBp65, ErbB3;

(d) PR, NME1, XIAP, upa, cyclinG1, Contig51037, TERC, EPHX1, ALDH1A3, CTSL;

(e) CA9, NME1, TERC, cyclinG1, EPHX1, DPYD, Src, TOP2B, NFKBp65, VEGFC;

(f) TFRC, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, ErbB3, NFKBp65;

(g) Bcl2, PRAME, cyclinG1, FOXM1, NFKBp65, TS, XIAP, Ki67, CYP3A4, p27;

(h) FOXM1, cyclinG1, XIAP, Contig51037, PRAME, TS, Ki67, PDGFRa, p27, NFKBp65;

(i) PRAME, FOXM1, cyclinG1, XIAP, Contig51037, TS, Ki6, PDGFRa, p27, NFKBp65;

(j) Ki67, XIAP, PRAME, hENT1, contig51037, TS, CD9, p27, ErbB3, cyclinG1;

(k) STK15, XIAP, PRAME, PLAUR, p27, CTSL, CD18, PREP, p53, RPS6KB1;

(l) GSTM1, XIAP, PRAME, p27, Contig51037, ErbB3, GSTp, EREG, ID1, PLAUR;

(m) PR, PRAME, NME1, XIAP, PLAUR, cyclinG1, Contig51037, TERC, EPHX1, DR5;

(n) CA9, FOXM1, cyclinG1, XIAP, TS, Ki67, NFKBp65, CYP3A4, GSTM3, p27;

(o) TFRC, XIAP, PRAME, p27, Contig51037, ErbB3, DPYD, TERC, NME1, VEGFC; and

(p) CEGP1, PRAME, hENT1, XIAP, Contig51037, ErbB3, DPYD, NFKBp65, ID1, TS

in a breast cancer tissue sample obtained from said patient, normalized against the expression levels of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products;

(2) subjecting the data obtained in step (a) to statistical analysis; and

(3) determining whether the likelihood of said long-term survival has increased or decreased.

42. A method of predicting the likelihood of long-term survival of a patient diagnosed with estrogen receptor (ER)-positive invasive breast cancer, without the recurrence of breast cancer, following surgical removal of the primary tumor, comprising the steps of:

(1) determining the expression levels of the RNA transcripts or the expression products of genes of a gene set selected from the group consisting of

(a) PRAME, p27, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(b) Contig51037, EPHX1, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(c) Bcl2, hENT1, FOXM1, Contig51037, cyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(d) HIF1A, PRAME, p27, IGFBP2, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(e) IGF1R, PRAME, EPHX1, Contig51037, cyclinG1, Bcl2, NME1, PTEN, TBP, TIMP2;

(f) FOXM1, Contig51037, VEGFC, TBP, HIF1A, DPYD, RAD51C, DCR3, cyclinG1, BAG1;

(g) EPHX1, Contig51037, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(h) Ki67, VEGFC, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(i) CDC25B, Contig51037, hENT1, Bcl2, HLAG, TERC, NME1, upa, ID1, CYP;

(j) VEGFC, Ki67, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(k) CTSB, PRAME, p27, IGFBP2, EPHX1, CTSL, BAD, DR5, DCR3, XIAP;

(l) DIABLO, Ki67, hENT1, TIMP2, ID1, p27, KRT19, IGFBP2, TS, PDGFB;

(m) p27, PRAME, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(n) CDH1; PRAME, VEGFC; HIF1A; DPYD, TIMP2, CYP3A4, EstR1, RBP4, p27;

(o) IGFBP3, PRAME, p27, Bcl2, XIAP, EstR1, Ki67, TS, Src, VEGF;

(p) GSTM3, PRAME, p27, IGFBP3, XIAP, FGF2, hENT1, PTEN, EstR1, APC;

(q) hENT1, Bcl2, FOXM1, Contig51037, CyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(r) STK15, VEGFC, PRAME, p27, GCLC, hENT1, ID1, TIMP2, EstR1, MCP1;

(s) NME1, PRAM, p27, IGFBP3, XIAP, PTEN, hENT1, Bcl2, CYP3A4, HLAG;

(t) VDR, Bcl2, p27, hENT1, p53, PI3KC2A, EIF4E, TFRC, MCM3, ID1;

(u) EIF4E, Contig51037, EPHX1, cyclinG1, Bcl2, DR5, TBP, PTEN, NME1, HER2;

(v) CCNB1, PRAME, VEGFC, HIF1A, hENT1, GCLC, TIMP2, ID1, p27, upa;

(w) ID1, PRAME, DIABLO, hENT1, p27, PDGFRa, NME1, BIN1, BRCA1, TP;

(x). FBXO5, PRAME, IGFBP3, p27, GSTM3, hENT1, XIAP, FGF2, TS, PTEN;

(y) GUS, HIA1A, VEGFC, GSTM3, DPYD, hENT1, EBXO5, CA9, CYP, KRT18; and

(z) Bclx, Bcl2, hENT1, Contig51037, HLAG, CD9, ID1, BRCA1, BIN1, HBEGF;

(2) subjecting the data obtained in step (1) to statistical analysis; and

(3) determining whether the likelihood of said long-term survival has increased or decreased.

43. The method of claim 41 or claim 42 wherein said statistical analysis is performed by using the Cox Proportional Hazards model.

44. An array comprising polynucleotides hybridizing to a gene set selected from the group consisting of

(a) Bcl2, cyclinG1, NFKBp65, NME1, EPHX1, TOP2B, DR5, TERC, Src, DIABLO;

(b) Ki67, XIAP, hENT1, TS, CD9, p27, cyclinG1, pS2, NFKBp65, CYP3A4;

(c) GSTM1, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, NFKBp65, ErbB3;

(d) PR, NME1, XIAP, upa, cyclinG1, Contig51037, TERC, EPHX1, ALDH1A3, CTSL;

(e) CA9, NME1, TERC, cyclinG1, EPHX1, DPYD, Src, TOP2B, NFKBp65, VEGFC;

(f) TFRC, XIAP, Ki67, TS, cyclinG1, p27, CYP3A4, pS2, ErbB3, NFKBp65;

(g) Bcl2, PRAME, cyclinG1, FOXM1, NFKBp65, TS, XIAP, Ki67, CYP3A4, p27;

(h) FOXM1, cyclinG1, XIAP, Contig51037, PRAME, TS, Ki67, PDGFRa, p27, NFKBp65;

(i) PRAME, FOXM1, cyclinG1, XIAP, Contig51037, TS, Ki6, PDGFRa, p27, NFKBp65;

(j) Ki67, XIAP, PRAME, hENT1, contig51037, TS, CD9, p27, ErbB3, cyclinG1;

(k) STK15, XIAP, PRAME, PLAUR, p27, CTSL, CD18, PREP, p53, RPS6KB1;

(l) GSTM1, XIAP, PRAME, p27, Contig51037, ErbB3, GSTp, EREG, ID1, PLAUR;

(m) PR, PRAME, NME1, XIAP, PLAUR, cyclinG1, Contig51037, TERC, EPHX1, DR5;

(n) CA9, FOXM1, cyclinG1, XIAP, TS, Ki67, NFKBp65, CYP3A4, GSTM3, p27;

(o) TFRC, XIAP, PRAME, p27, Contig51037, ErbB3, DPYD, TERC, NME1, VEGFC; and

(p) CEGP1, PRAME, hENT1, XIAP, Contig51037, ErbB3, DPYD, NFKBp65, ID1, TS,

immobilized on a solid surface.

45. An array comprising polynucleotides hybridizing to a gene set selected from the group consisting of

(a) PRAME, p27, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(b) Contig51037, EPHX1, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(c) Bcl2, hENT1, FOXM1, Contig51037, cyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(d) HIF1A, PRAME, p27, IGFBP2, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(e) IGF1R, PRAME, EPHX1, Contig51037, cyclinG1, Bcl2, NME1, PTEN, TBP, TIMP2;

(f) FOXM1, Contig51037, VEGFC, TBP, HIF1A, DPYD, RAD51C, DCR3, cyclinG1, BAG1;

(g) EPHX1, Contig51037, Ki67, TIMP2, cyclinG1, DPYD, CYP3A4, TP, AIB1, CYP2C8;

(h) Ki67, VEGFC, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(i) CDC25B, Contig51037, hENT1, Bcl2, HLAG, TERC, NME1, upa, ID1, CYP;

(j) VEGFC, Ki67, VDR, GSTM3, p27, upa, ITGA7, rhoC, TERC, Pin1;

(k) CTSB, PRAME, p27, IGFBP2, EPHX1, CTSL, BAD, DR5, DCR3, XIAP;

(l) DIABLO, Ki67, hENT1, TIMP2, ID1, p27, KRT19, IGFBP2, TS, PDGFB;

(m) p27, PRAME, IGFBP2, HIF1A, TIMP2, ILT2, CYP3A4, ID1, EstR1, DIABLO;

(n) CDH1; PRAME, VEGFC; HIF1A; DPYD, TIMP2, CYP3A4, EstR1, RBP4, p27;

(o) IGFBP3, PRAME, p27, Bcl2, XIAP, EstR1, Ki67, TS, Src, VEGF;

(p) GSTM3, PRAME, p27, IGFBP3, XIAP, FGF2, hENT1, PTEN, EstR1, APC;

(q) hENT1, Bcl2, FOXM1, Contig51037, CyclinG1, Contig46653, PTEN, CYP3A4, TIMP2, AREG;

(r) STK15, VEGFC, PRAME, p27, GCLC, hENT1, ID1, TIMP2, EstR1, MCP1;

(s) NME1, PRAM, p27, IGFBP3, XIAP, PTEN, hENT1, Bcl2, CYP3A4, HLAG;

(t) VDR, Bcl2, p27, hENT1, p53, PI3KC2A, EIF4E, TFRC, MCM3, ID1;

(u) EIF4E, Contig51037, EPHX1, cyclinG1, Bcl2, DR5, TBP, PTEN, NME1, HER2;

(v) CCNB1, PRAME, VEGFC, HIF1A, hENT1, GCLC, TIMP2, ID1, p27, upa;

(w) ID1, PRAME, DIABLO, hENT1, p27, PDGFRa, NME1, BIN1, BRCA1, TP;

(x) FBXO5, PRAME, IGFBP3, p27, GSTM3, hENT1, XIAP, FGF2, TS, PTEN;

(y) GUS, HIA1A, VEGFC, GSTM3, DPYD, hENT1, FBXO5, CA9, CYP, KRT18; and

(z) Bclx, Bcl2, hENT1, Contig51037, HLAG, CD9, ID1, BRCA1, BIN1, HBEGF,

immobilized on a solid surface.

Overall FPET/RT-PCR Flow Chart

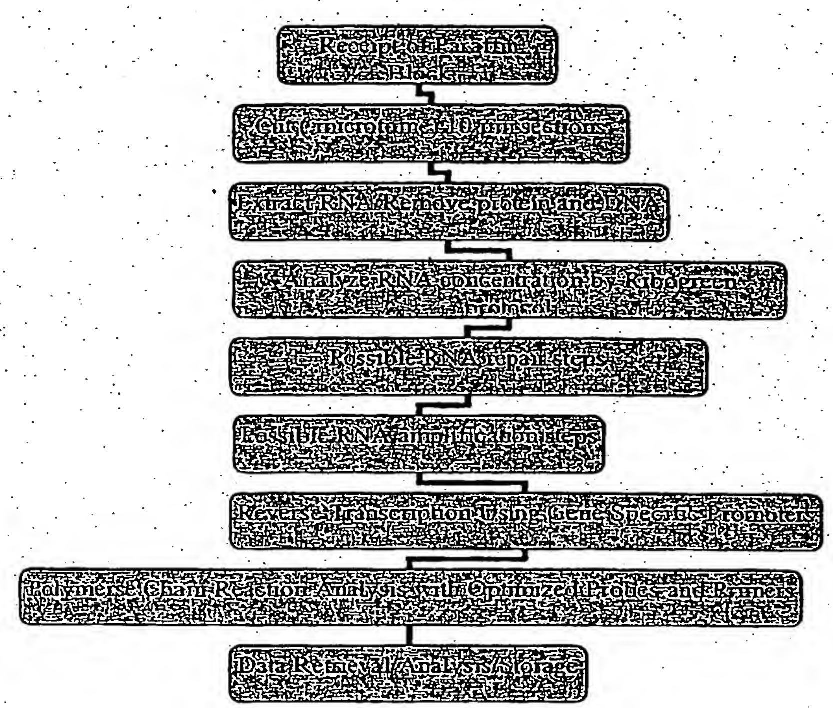


FIGURE 1

Process Definition - Flow Chart 1
RNA Isolation from FPET Blocks

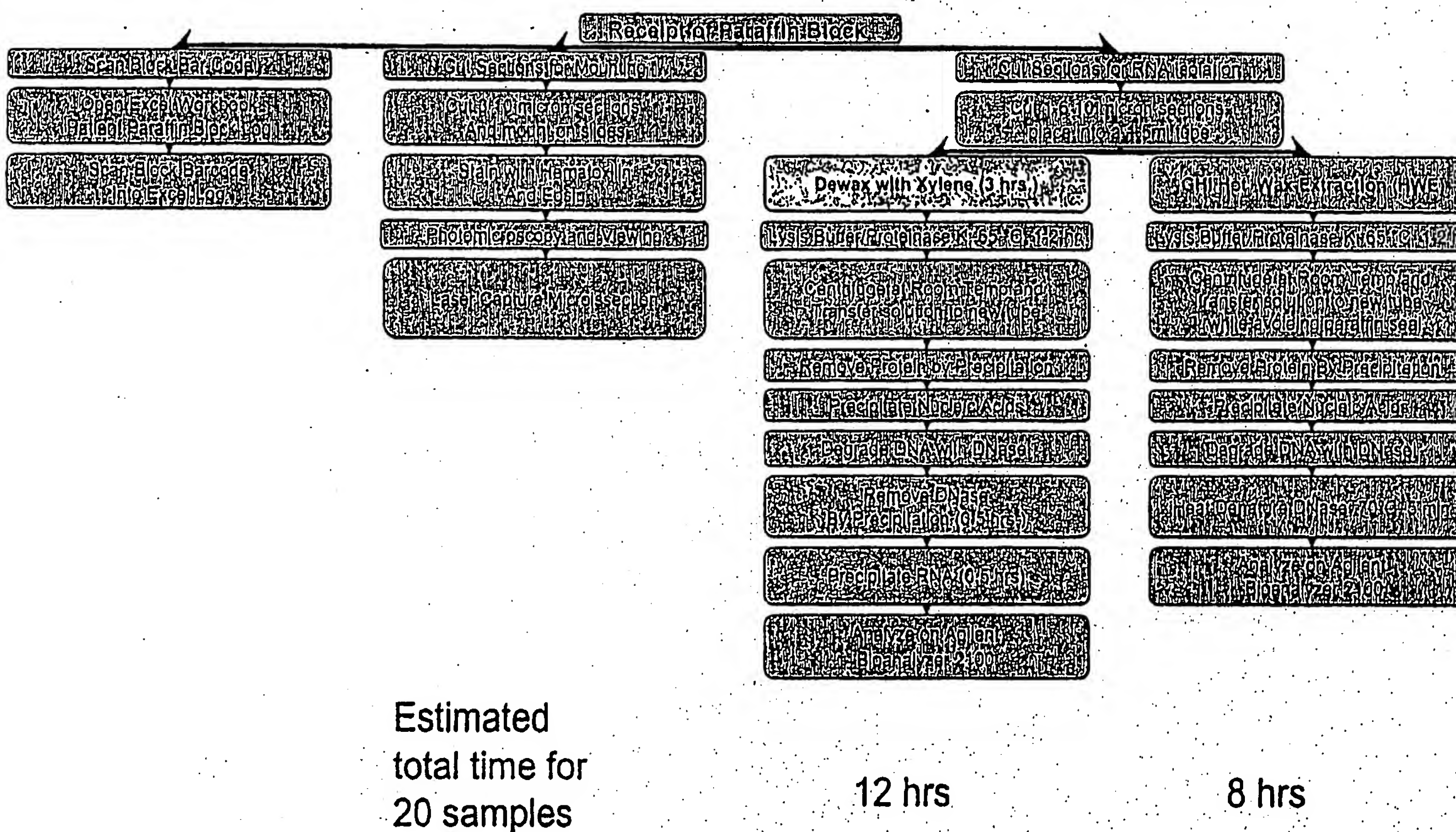


FIGURE 2

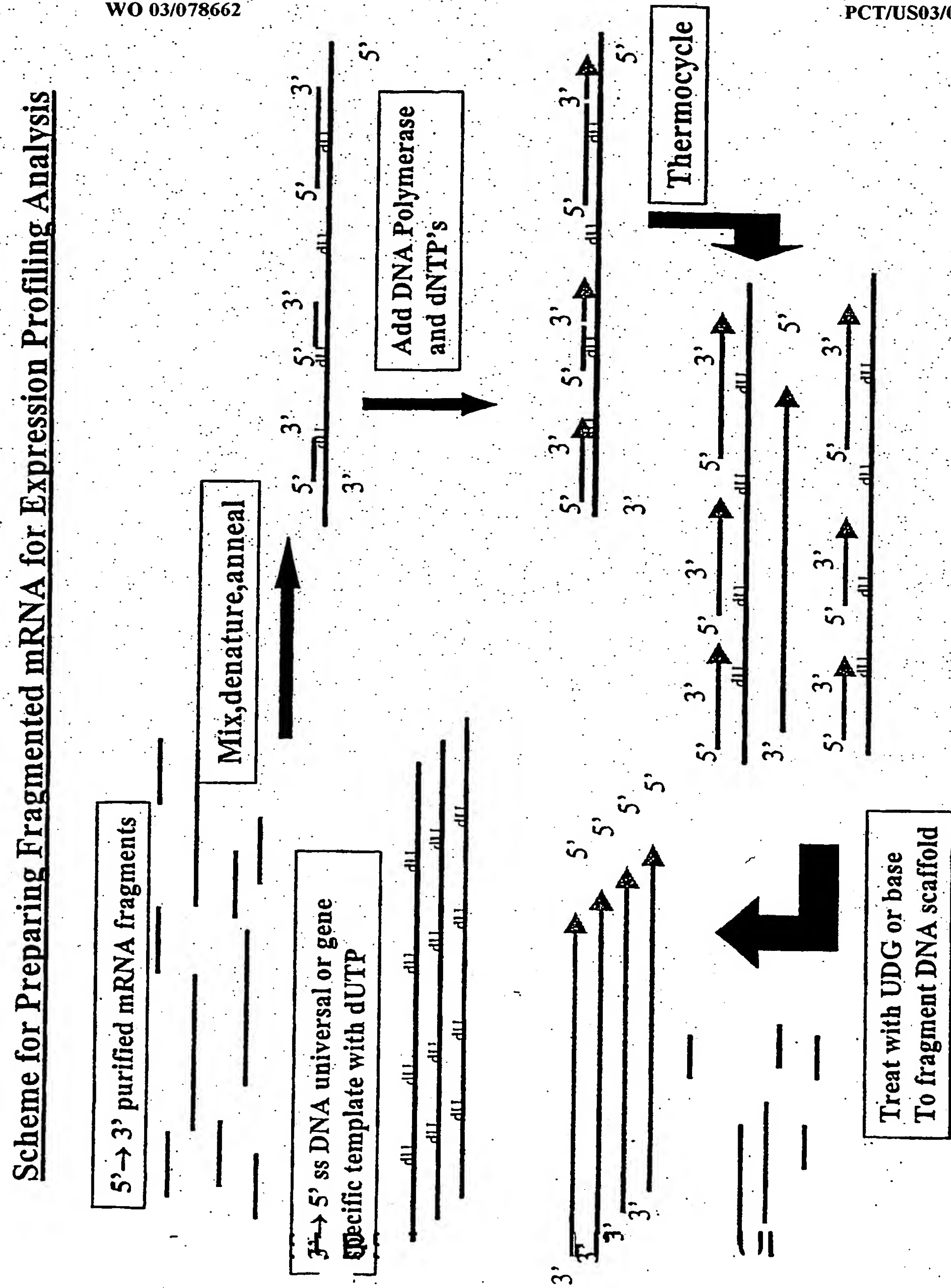
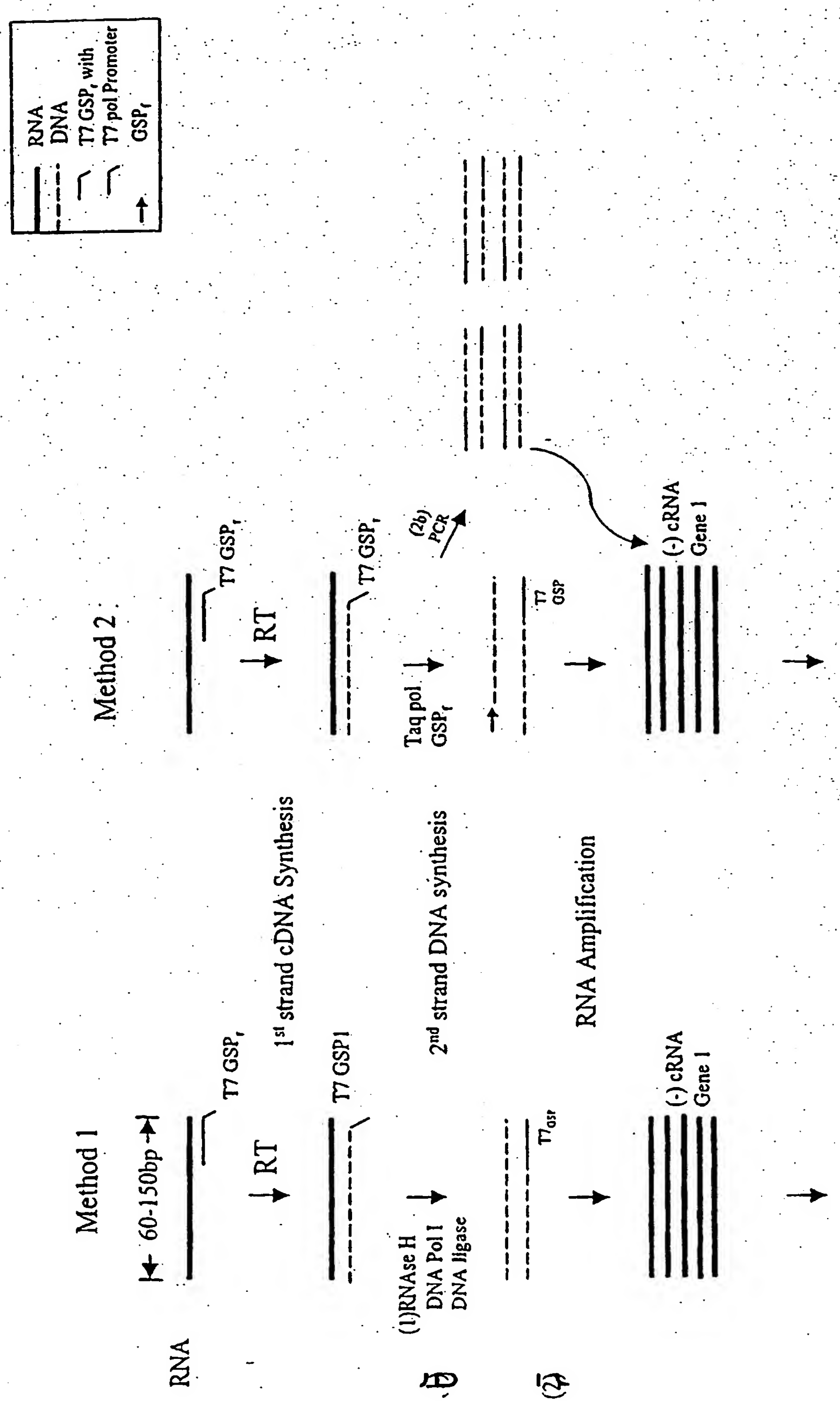


FIGURE 3

SUBSTITUTE SHEET (RULE 26)



RT-PCR (one-step or two-step)

FIGURE 4

Alternative Scheme for Preparing Fragmented mRNA for Expression Profiling Analysis

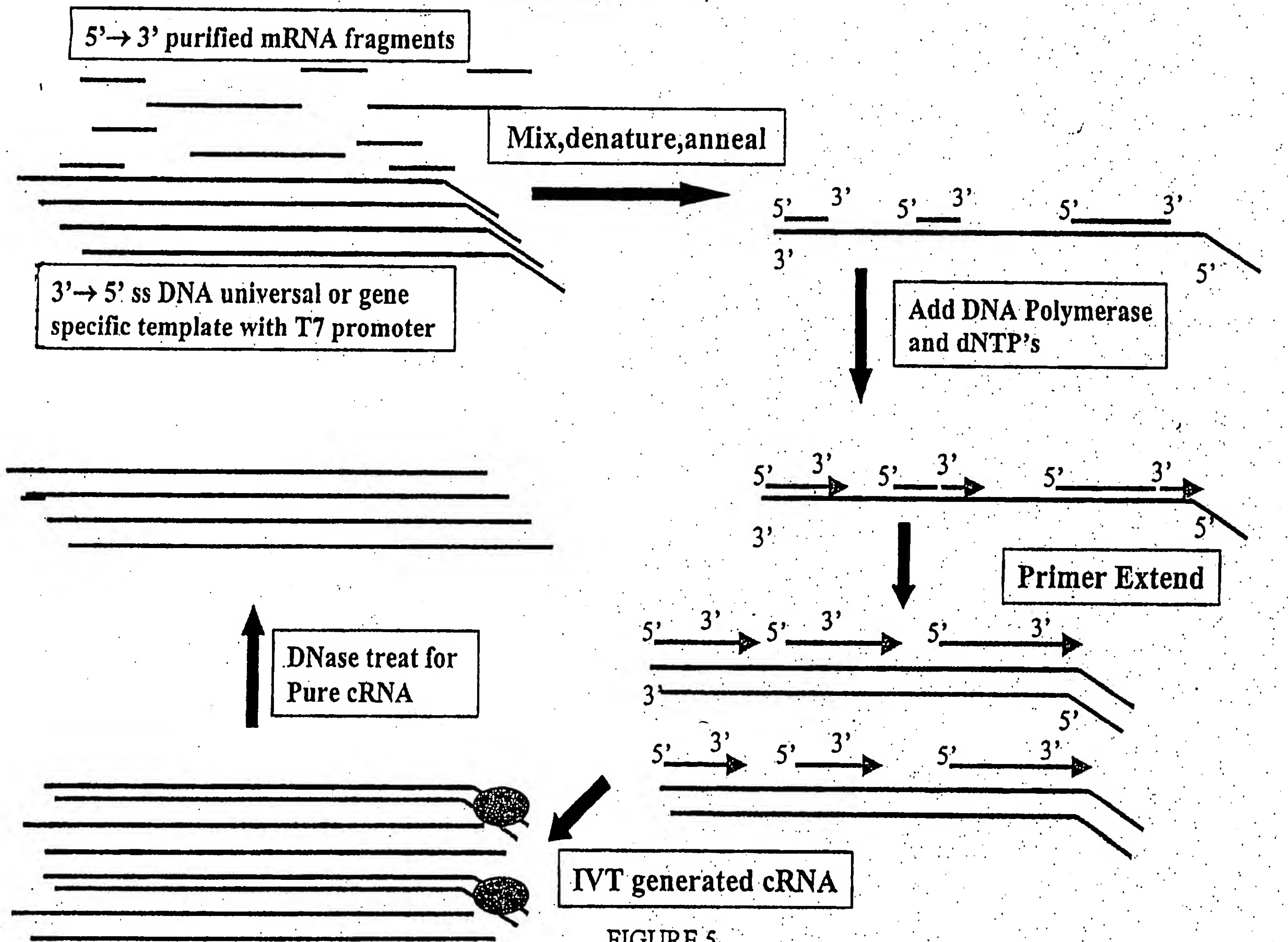


FIGURE 5

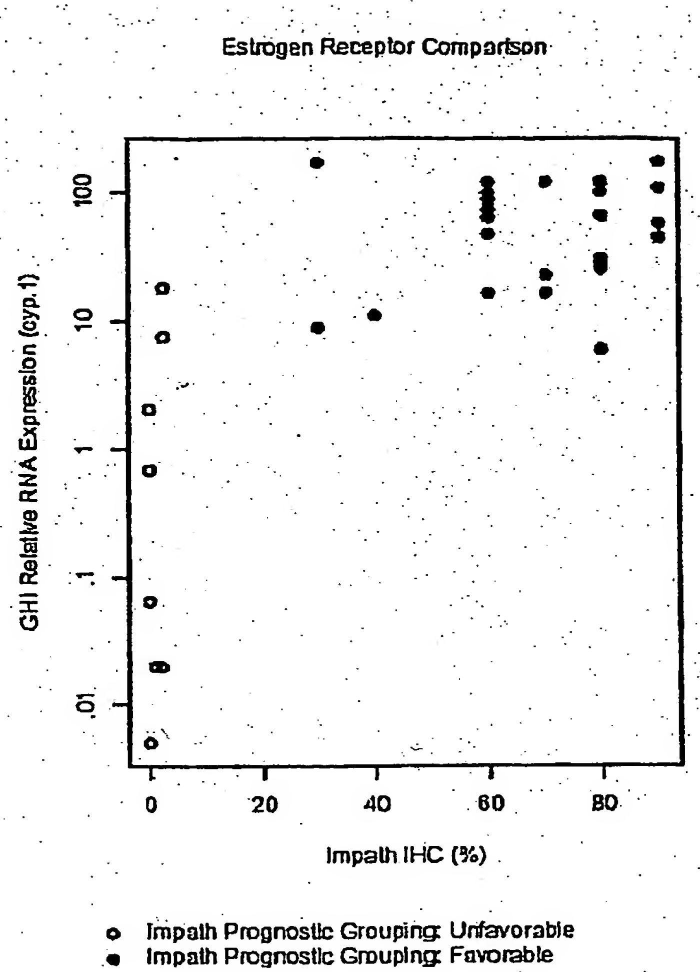

Estrogen Receptor Comparison
GHI Relative RNA Expression (cyp.1)
100
10
1
.1
.01
0
20
40
60
80
Impath IHC (%)
Impath Prognostic Grouping: Unfavorable
Impath Prognostic Grouping: Favorable

FIGURE 6

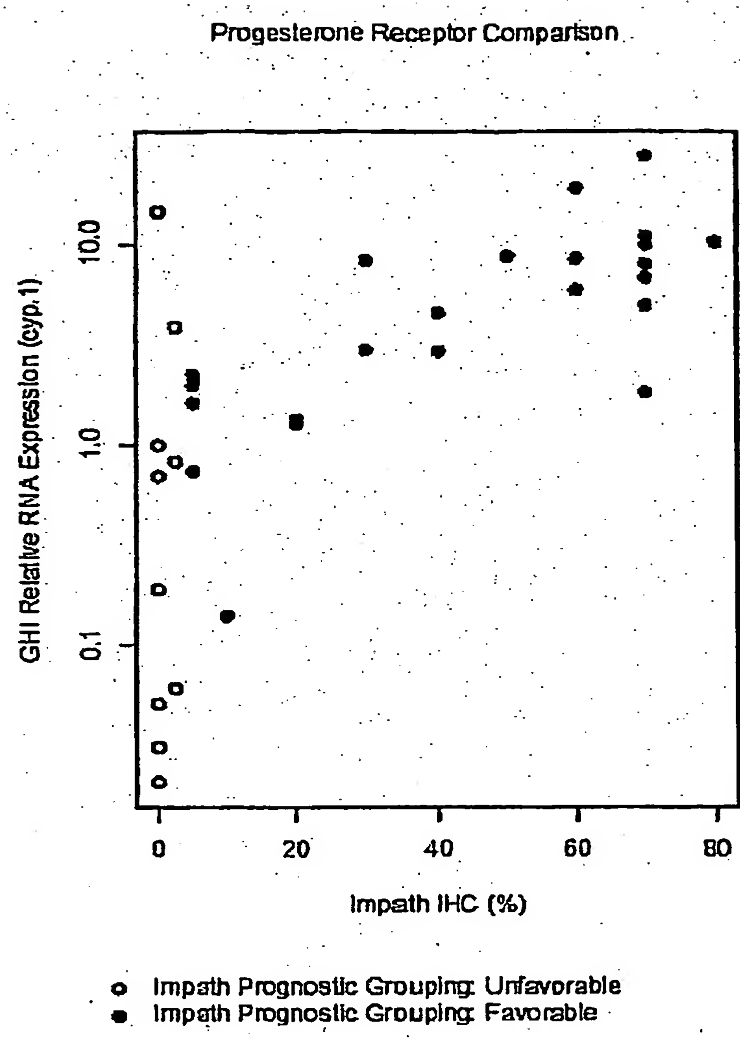

Progesterone Receptor Comparison
GHI Relative RNA Expression (cyp.1)
10.0
1.0
0.1
0
20
40
60
80
Impath IHC (%)
Impath Prognostic Grouping: Unfavorable
Impath Prognostic Grouping: Favorable

FIGURE 7

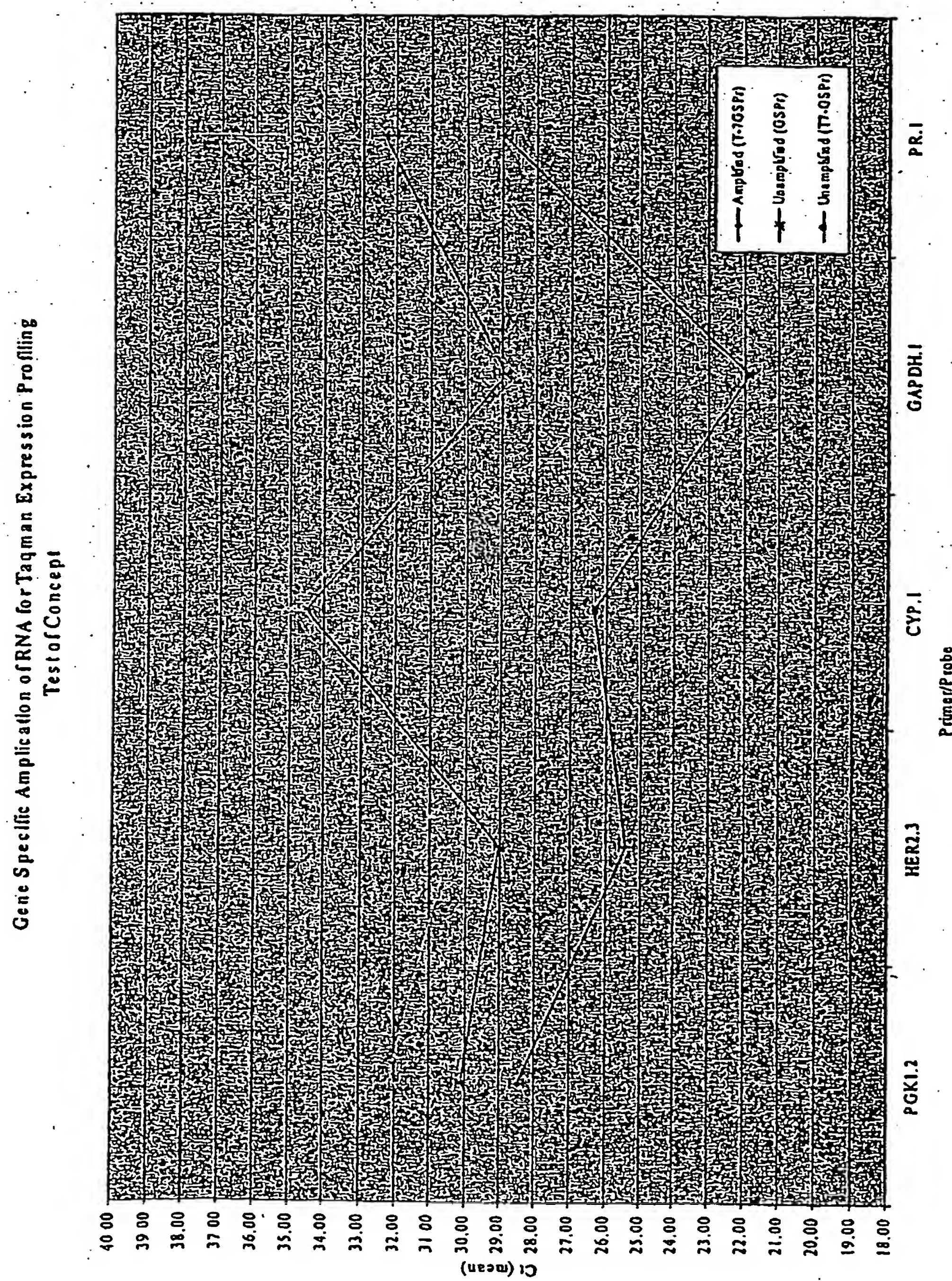
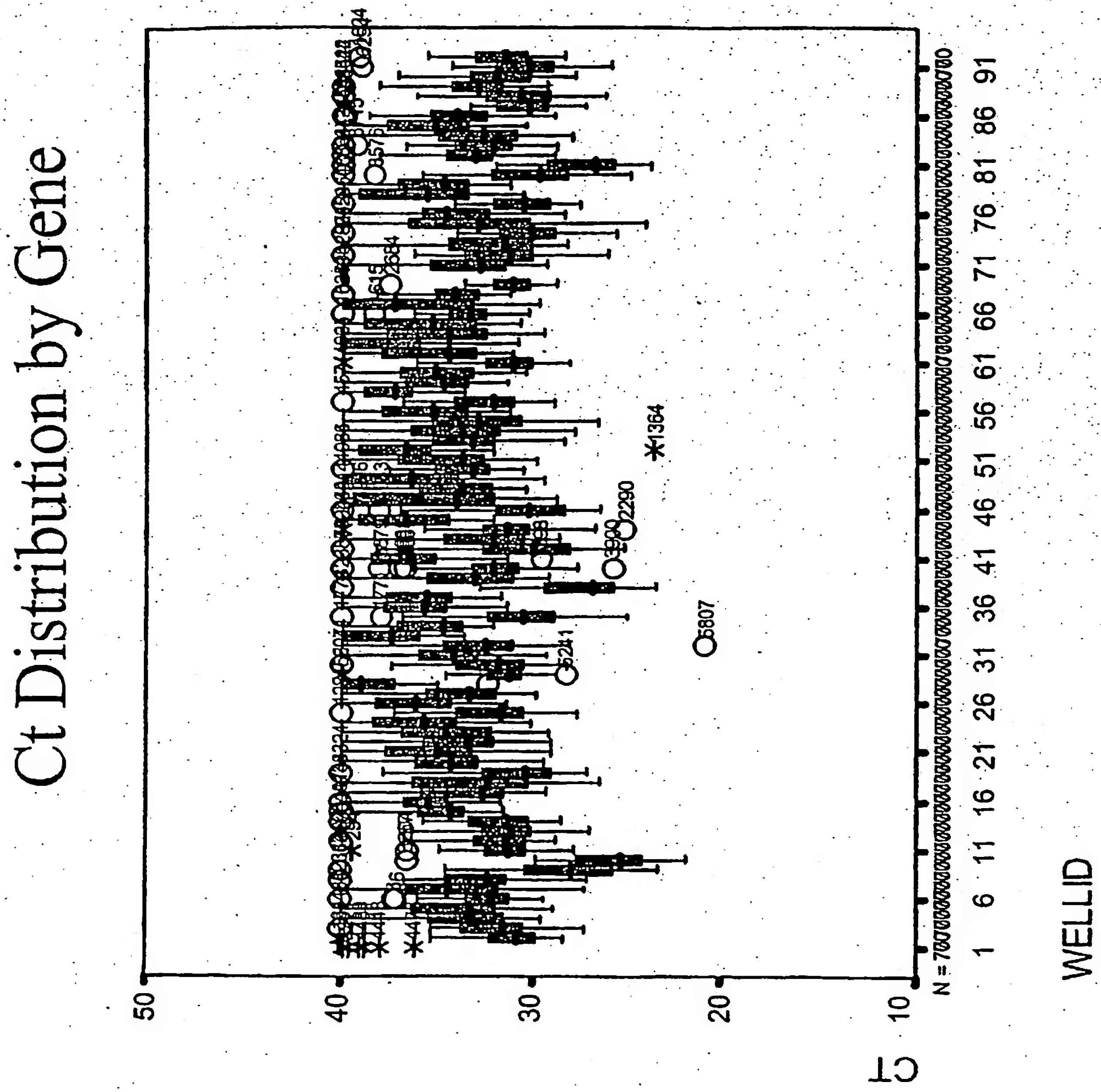

Gene Specific Amplification of RNA for Taqman Expression Profiling
Test of Concept
Amplified (T7-GSPr)
Unamplified (GSPr)
Unamplified (T7-GSPr)
PGK1.2
HER2.3
CYP.1
GAPDH.1
PR.1
Primer/Probe
Ct (mean)
40.00
39.00
38.00
37.00
36.00
35.00
34.00
33.00
32.00
31.00
30.00
29.00
28.00
27.00
26.00
25.00
24.00
23.00
22.00
21.00
20.00
19.00
18.00

Figure 8

FIGURE 9



SUBSTITUTE SHEET (RULE 26)

39740-0001PCT.txt

SEQUENCE LISTING

<110> GENOMIC HEALTH
Baker, Joffre B.
Cronin, Maureen T.
Kiefer, Michael C.
Shak, Steve
Walker, Michael Graham

<120> GENE EXPRESSION PROFILING IN BIOPSIED TUMOR TISSUES

<130> 39740-0001PCT

<140> to be assigned
<141> 2003-03-12

<150> US 60/412,049
<151> 2002-09-18

<150> US 60/364,890
<151> 2002-03-13

<160> 384

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 18
<212> DNA
<213> Homo sapiens

<400> 1
gtcccaggag cccatcct 18

<210> 2
<211> 19
<212> DNA
<213> Homo sapiens

<400> 2
cccggctgtt gtctccata 19

<210> 3
<211> 68
<212> DNA
<213> Homo sapiens

<400> 3
gtcccaggag cccatcctgt ttgactgcag cattgctgag aacattgcct atggagacaa 60
cagccggg 68

<210> 4
<211> 18
<212> DNA
<213> Homo sapiens

<400> 4
tcatggtgcc cgtcaatg 18

<210> 5
<211> 23
<212> DNA
<213> Homo sapiens

<400> 5
cgattgtctt tgctcttcat gtg 23

<210> 6
<211> 79
<212> DNA
<213> Homo sapiens

<400> 6
tcatggtgcc cgtcaatgct gtgatggcga tgaagaccaa gacgtatcag gtggcccaca 60
tgaagagcaa agacaatcg 79

<210> 7
<211> 20
<212> DNA
<213> Homo sapiens

<400> 7
aggggatgac ttggacacat 20

<210> 8
<211> 20
<212> DNA
<213> Homo sapiens

<400> 8
aaaactgcat ggctttgtca 20

<210> 9
<211> 65
<212> DNA
<213> Homo sapiens

<400> 9
aggggatgac ttggacacat ctgccattcg acatgactgc aattttgaca aagccatgca 60
gtttt 65

<210> 10
<211> 22
<212> DNA
<213> Homo sapiens

<400> 10
tcatcctggc gatctacttc ct 22

<210> 11
<211> 20
<212> DNA
<213> Homo sapiens

<400> 11
ccgttgagtg gaatcagcaa 20

<210> 12
<211> 91
<212> DNA
<213> Homo sapiens

<400> 12
tcatcctggc gatctacttc ctctggcaga acctaggtcc ctctgtcctg gctggagtcg 60
ctttcatggt cttgctgatt ccactcaacg g 91

<210> 13
<211> 20
<212> DNA
<213> Homo sapiens

<400> 13
agcgcctgga atctacaact 20

<210> 14
<211> 20
<212> DNA
<213> Homo sapiens

<400> 14
agagcccctg gagagaagat 20

<210> 15
<211> 66
<212> DNA
<213> Homo sapiens

<400> 15
agcgcctgga atctacaact cggagtccag tgttttccca cttgtcatct tctctccagg 60
ggctct 66

<210> 16
<211> 24
<212> DNA
<213> Homo sapiens

<400> 16
gcccagagaa ggtctatgaa ctca 24

<210> 17
<211> 22
<212> DNA
<213> Homo sapiens

<400> 17
gtttcaaagg cttggtggat tt 22

<210> 18
<211> 94
<212> DNA
<213> Homo sapiens

<400> 18
gcccagagaa ggtctatgaa ctcatgcgag catgttggca gtggaatccc tctgaccggc 60
cctcctttgc tgaaatccac caagcctttg aaac 94

<210> 19
<211> 21
<212> DNA
<213> Homo sapiens

<400> 19
cgcagtgcag ctgagtatct g 21

<210> 20
<211> 21
<212> DNA
<213> Homo sapiens

<400> 20
tgcccagggc tactctcact t 21

<210> 21
<211> 80
<212> DNA
<213> Homo sapiens

<400> 21
cgcagtgcag ctgagtatct gctcagcagt ctaatcaatg gcagcttcct ggtgcgagaa 60
agtgagagta gccctgggca 80

<210> 22

<211> 21
<212> DNA
<213> Homo sapiens

<400> 22
cagcagatgt ggatcagcaa g 21

<210> 23
<211> 18
<212> DNA
<213> Homo sapiens

<400> 23
gcatttgcgg tggacgat 18

<210> 24
<211> 66
<212> DNA
<213> Homo sapiens

<400> 24
cagcagatgt ggatcagcaa gcaggagtat gacgagtccg gcccctccat cgtccaccgc 60
aaatgc 66

<210> 25
<211> 20
<212> DNA
<213> Homo sapiens

<400> 25
cgcttctatg gcgctgagat 20

<210> 26
<211> 20
<212> DNA
<213> Homo sapiens

<400> 26
tcccggtaca ccacgttctt 20

<210> 27
<211> 71
<212> DNA
<213> Homo sapiens

<400> 27
cgcttctatg gcgctgagat tgtgtcagcc ctggactacc tgcactcgga gaagaacgtg 60
gtgtaccggg a 71

<210> 28
<211> 25
<212> DNA
<213> Homo sapiens

<400> 28
ttgtctctgc cttggactat ctaca 25

<210> 29
<211> 24
<212> DNA
<213> Homo sapiens

<400> 29
ccagcattag attctccaac ttga 24

<210> 30
<211> 75
<212> DNA

<213> Homo sapiens

<400> 30
ttgtctctgc cttggactat ctacattccg gaaagattgt gtaccgtgat ctcaagttgg 60
agaatctaat gctgg 75

<210> 31
<211> 25
<212> DNA
<213> Homo sapiens

<400> 31
gaaggagata aggaggatgt tgaca 25

<210> 32
<211> 18
<212> DNA
<213> Homo sapiens

<400> 32
cgccacggag atccaatc 18

<210> 33
<211> 74
<212> DNA
<213> Homo sapiens

<400> 33
gaaggagata aggaggatgt tgacaaggca gtgaaggccg caagacaggc ttttcagatt 60
ggatctccgt ggcg 74

<210> 34
<211> 21
<212> DNA
<213> Homo sapiens

<400> 34
tggtgaacat tgtgccagga t 21

<210> 35
<211> 22
<212> DNA
<213> Homo sapiens

<400> 35
gaaggcgatc ttgttgatct ga 22

<210> 36
<211> 80
<212> DNA
<213> Homo sapiens

<400> 36
tggtgaacat tgtgccagga ttcgggccca cagtgggagc agcaatttct tctcaccctc 60
agatcaacaa gatcgccttc 80

<210> 37
<211> 20
<212> DNA
<213> Homo sapiens

<400> 37
ggacagcagg aatgtgtttc 20

<210> 38
<211> 20
<212> DNA
<213> Homo sapiens

<400> 38
acccactcga tttgtttctg 20

<210> 39
<211> 69
<212> DNA
<213> Homo sapiens

<400> 39
ggacagcagg aatgtgtttc tccatacagg tcacggggag ccaatggttc agaaacaaat 60
cgagtgggt 69

<210> 40
<211> 27
<212> DNA
<213> Homo sapiens

<400> 40
tgtgagtgaa atgccttcta gtagtga 27

<210> 41
<211> 27
<212> DNA
<213> Homo sapiens

<400> 41
ttgtggttcg ttatcatact cttctga 27

<210> 42
<211> 82
<212> DNA
<213> Homo sapiens

<400> 42
tgtgagtgaa atgccttcta gtagtgaacc gtcctcggga gccgactatg actactcaga 60
agagtatgat aacgaaccac aa 82

<210> 43
<211> 19
<212> DNA
<213> Homo sapiens

<400> 43
gtctcgctcc gtggcctta 19

<210> 44
<211> 24
<212> DNA
<213> Homo sapiens

<400> 44
cgtgagtaaa cctgaatctt tgga 24

<210> 45
<211> 93
<212> DNA
<213> Homo sapiens

<400> 45
gtctcgctcc gtggccttag ctgtgctcgc gctactctct ctttctggcc tggaggctat 60
ccagcgtact ccaaagattc aggtttactc acg 93

<210> 46
<211> 20
<212> DNA
<213> Homo sapiens

<400> 46
ccattcccac cattctacct 20

<210> 47
<211> 20
<212> DNA
<213> Homo sapiens

<400> 47
gggaacatag acccaccaat 20

<210> 48
<211> 66
<212> DNA
<213> Homo sapiens

<400> 48
ccattcccac cattctacct gaggccagga cgtctggggt gtggggattg gtgggtctat 60
gttccc 66

<210> 49
<211> 18
<212> DNA
<213> Homo sapiens

<400> 49
ccgccgtgga cacagact 18

<210> 50
<211> 21
<212> DNA
<213> Homo sapiens

<400> 50
ttgccgtcag aaaacatgtc a 21

<210> 51
<211> 70
<212> DNA
<213> Homo sapiens

<400> 51
ccgccgtgga cacagactcc ccccgagagg tctttttccg agtggcagct gacatgtttt 60
ctgacggcaa 70

<210> 52
<211> 25
<212> DNA
<213> Homo sapiens

<400> 52
cagatggacc tagtacccac tgaga 25

<210> 53
<211> 24
<212> DNA
<213> Homo sapiens

<400> 53
cctatgattt aagggcattt ttcc 24

<210> 54
<211> 73
<212> DNA
<213> Homo sapiens

<400> 54
cagatggacc tagtacccac tgagatttcc acgccgaagg acagcgatgg gaaaaatgcc 60

cttaaatcat agg 73

<210> 55
<211> 24
<212> DNA
<213> Homo sapiens

<400> 55
cttttgtgga actctatggg aaca 24

<210> 56
<211> 19
<212> DNA
<213> Homo sapiens

<400> 56
cagcggttga agcgttcct 19

<210> 57
<211> 70
<212> DNA
<213> Homo sapiens

<400> 57
cttttgtgga actctatggg aacaatgcag cagccgagag ccgaaagggc caggaacgct 60
tcaaccgctg 70

<210> 58
<211> 24
<212> DNA
<213> Homo sapiens

<400> 58
ggatatttcc gtggctctta ttca 24

<210> 59
<211> 25
<212> DNA
<213> Homo sapiens

<400> 59
cttctcatca aggcagaaaa atctt 25

<210> 60
<211> 86
<212> DNA
<213> Homo sapiens

<400> 60
ggatatttcc gtggctctta ttcaaactct ccatcaaatc ctgtaaactc cagagcaaat 60
caagattttt ctgccttgat gagaag 86

<210> 61
<211> 23
<212> DNA
<213> Homo sapiens

<400> 61
gcagttggaa gacacaggaa agt 23

<210> 62
<211> 21
<212> DNA
<213> Homo sapiens

<400> 62
tgcgtggcac tattttcaag a 21

<210> 63
<211> 77
<212> DNA
<213> Homo sapiens

<400> 63
gcagttggaa gacacaggaa agtatcccca aattgcagat ttatcaacgg cttttatctt 60
gaaaatagtg ccacgca 77

<210> 64
<211> 20
<212> DNA
<213> Homo sapiens

<400> 64
tgttttgatt cccgggctta 20

<210> 65
<211> 24
<212> DNA
<213> Homo sapiens

<400> 65
caaagctgtc agctctagca aaag 24

<210> 66
<211> 80
<212> DNA
<213> Homo sapiens

<400> 66
tgttttgatt cccgggctta ccaggtgaga agtgagggag gaagaaggca gtgtcccttt 60
tgctagagct gacagctttg 80

<210> 67
<211> 20
<212> DNA
<213> Homo sapiens

<400> 67
tcaggggct agaaatctgt 20

<210> 68
<211> 20
<212> DNA
<213> Homo sapiens

<400> 68
ccattccagt tgatctgtgg 20

<210> 69
<211> 65
<212> DNA
<213> Homo sapiens

<400> 69
tcaggggct agaaatctgt tgctatgggc ccttcaccaa catgcccaca gatcaactgg 60
aatgg 65

<210> 70
<211> 20
<212> DNA
<213> Homo sapiens

<400> 70
agttcgtgct ttgcaagatg 20

<210> 71

<211> 20
<212> DNA
<213> Homo sapiens

<400> 71
aaggtaagct gggtctgctg 20

<210> 72
<211> 70
<212> DNA
<213> Homo sapiens

<400> 72
agttcgtgct ttgcaagatg gtgcagagct ttatgaagca gtgaagaatg cagcagaccc 60
agcttacctt 70

<210> 73
<211> 21
<212> DNA
<213> Homo sapiens

<400> 73
gcatgttcgt ggcctctaag a 21

<210> 74
<211> 22
<212> DNA
<213> Homo sapiens

<400> 74
cggtgtagat gcacagcttc tc 22

<210> 75
<211> 69
<212> DNA
<213> Homo sapiens

<400> 75
gcatgttcgt ggcctctaag atgaaggaga ccatccccct gacggccgag aagctgtgca 60
tctacaccg 69

<210> 76
<211> 20
<212> DNA
<213> Homo sapiens

<400> 76
agatgaagtg gaaggcgctt 20

<210> 77
<211> 21
<212> DNA
<213> Homo sapiens

<400> 77
tgcctctgta atcggcaact g 21

<210> 78
<211> 65
<212> DNA
<213> Homo sapiens

<400> 78
agatgaagtg gaaggcgctt ttcaccgcgg ccatcctgca ggcacagttg ccgattacag 60
aggca 65

<210> 79
<211> 18

<212> DNA
<213> Homo sapiens

<400> 79
tggttcccag ccctgtgt 18

<210> 80
<211> 19
<212> DNA
<213> Homo sapiens

<400> 80
ctcctccacc ctgggttgt 19

<210> 81
<211> 74
<212> DNA
<213> Homo sapiens

<400> 81
tggttcccag ccctgtgtcc acctccaagc ccagattcag attcgagtca tgtacacaac 60
ccagggtgga ggag 74

<210> 82
<211> 20
<212> DNA
<213> Homo sapiens

<400> 82
tcttgctggc tacgcctctt 20

<210> 83
<211> 21
<212> DNA
<213> Homo sapiens

<400> 83
ctgcattgtg gcacagttct g 21

<210> 84
<211> 71
<212> DNA
<213> Homo sapiens

<400> 84
tcttgctggc tacgcctctt ctgtccctgt tagacgtcct ccgtccatat cagaactgtg 60
ccacaatgca g 71

<210> 85
<211> 21
<212> DNA
<213> Homo sapiens

<400> 85
tgagtgtccc ccggtatctt c 21

<210> 86
<211> 21
<212> DNA
<213> Homo sapiens

<400> 86
cagccgcttt cagattttca t 21

<210> 87
<211> 81
<212> DNA
<213> Homo sapiens

<400> 87
tgagtgtccc ccggtatctt ccccgccctg ccaatcccga tgaaattgga aattttattg 60
atgaaaatct gaaagcggct g 81

<210> 88
<211> 21
<212> DNA
<213> Homo sapiens

<400> 88
tggagactct cagggtcgaa a 21

<210> 89
<211> 22
<212> DNA
<213> Homo sapiens

<400> 89
ggcgtttgga gtggtagaaa tc 22

<210> 90
<211> 65
<212> DNA
<213> Homo sapiens

<400> 90
tggagactct cagggtcgaa aacggcggca gaccagcatg acagatttct accactccaa 60
acgcc 65

<210> 91
<211> 21
<212> DNA
<213> Homo sapiens

<400> 91
cggtggacca cgaagagtta a 21

<210> 92
<211> 19
<212> DNA
<213> Homo sapiens

<400> 92
ggctcgcctc ttccatgtc 19

<210> 93
<211> 66
<212> DNA
<213> Homo sapiens

<400> 93
cggtggacca cgaagagtta acccgggact tggagaagca ctgcagagac atggaagagg 60
cgagcc 66

<210> 94
<211> 19
<212> DNA
<213> Homo sapiens

<400> 94
gcggaaggtc cctcagaca 19

<210> 95
<211> 23
<212> DNA
<213> Homo sapiens

<400> 95
tctaagtttc ccgaggtttc tca 23

<210> 96
<211> 70
<212> DNA
<213> Homo sapiens

<400> 96
gcggaaggtc cctcagacat ccccgattga aagaaccaga gaggctctga gaaacctcgg 60
gaaacttaga 70

<210> 97
<211> 22
<212> DNA
<213> Homo sapiens

<400> 97
ccagctttgt gcctgtcact at 22

<210> 98
<211> 20
<212> DNA
<213> Homo sapiens

<400> 98
gggaatgtgg tagcccaaga 20

<210> 99
<211> 71
<212> DNA
<213> Homo sapiens

<400> 99
ccagctttgt gcctgtcact attcctcatg ccaccactgc caacacctct gtcttgggct 60
accacattcc c 71

<210> 100
<211> 27
<212> DNA
<213> Homo sapiens

<400> 100
ttgctataac taagtgcttc tccaaga 27

<210> 101
<211> 22
<212> DNA
<213> Homo sapiens

<400> 101
gtggaatggc agctcactgt ag 22

<210> 102
<211> 73
<212> DNA
<213> Homo sapiens

<400> 102
ttgctataac taagtgcttc tccaagaccc caactgagtc cccagcacct gctacagtga 60
gctgccattc cac 73

<210> 103
<211> 19
<212> DNA
<213> Homo sapiens

<400> 103

aggacgcaag gagggtttg 19

<210> 104
<211> 21
<212> DNA
<213> Homo sapiens

<400> 104
gatgtccgcc gagtccttac t 21

<210> 105
<211> 87
<212> DNA
<213> Homo sapiens

<400> 105
aggacgcaag gagggtttgt cactggcaga ctcgagactg taggcactgc catggcccct 60
gtgctcagta aggactcggc ggacatc 87

<210> 106
<211> 24
<212> DNA
<213> Homo sapiens

<400> 106
ctatatgcag ccagagatgt gaca 24

<210> 107
<211> 24
<212> DNA
<213> Homo sapiens

<400> 107
ccacgagttt cttactgaga atgg 24

<210> 108
<211> 82
<212> DNA
<213> Homo sapiens

<400> 108
ctatatgcag ccagagatgt gacagccacc gtggacagcc tgccactcat cacagcctcc 60
attctcagta agaaactcgt gg 82

<210> 109
<211> 20
<212> DNA
<213> Homo sapiens

<400> 109
tgtcgatgga cttccagaac 20

<210> 110
<211> 19
<212> DNA
<213> Homo sapiens

<400> 110
attgggacag cttggatca 19

<210> 111
<211> 62
<212> DNA
<213> Homo sapiens

<400> 111
tgtcgatgga cttccagaac cacctgggca gctgccaaaa gtgtgatcca agctgtccca 60
at 62

<210> 112
<211> 23
<212> DNA
<213> Homo sapiens

<400> 112
gatctaagat ggcgactgtc gaa 23

<210> 113
<211> 25
<212> DNA
<213> Homo sapiens

<400> 113
ttagattccg ttttctcctc ttctg 25

<210> 114
<211> 82
<212> DNA
<213> Homo sapiens

<400> 114
gatctaagat ggcgactgtc gaaccggaaa ccacccctac tcctaatccc ccgactacag 60
aagaggagaa aacggaatct aa 82

<210> 115
<211> 20
<212> DNA
<213> Homo sapiens

<400> 115
cggtgtgaga agtgcagcaa 20

<210> 116
<211> 19
<212> DNA
<213> Homo sapiens

<400> 116
cctctcgcaa gtgctccat 19

<210> 117
<211> 70
<212> DNA
<213> Homo sapiens

<400> 117
cggtgtgaga agtgcagcaa gccctgtgcc cgagtgtgct atggtctggg catggagcac 60
ttgcgagagg 70

<210> 118
<211> 23
<212> DNA
<213> Homo sapiens

<400> 118
cggttatgtc atgccagata cac 23

<210> 119
<211> 24
<212> DNA
<213> Homo sapiens

<400> 119
gaactgagac ccactgaaga aagg 24

<210> 120

<211> 81
<212> DNA
<213> Homo sapiens

<400> 120
cggttatgtc atgccagata cacacctcaa aggtactccc tcctcccggg aaggcaccct 60
ttcttcagtg ggtctcagtt c 81

<210> 121
<211> 19
<212> DNA
<213> Homo sapiens

<400> 121
cgtggtgccc ctctatgac 19

<210> 122
<211> 19
<212> DNA
<213> Homo sapiens

<400> 122
ggctagtggg cgcatgtag 19

<210> 123
<211> 68
<212> DNA
<213> Homo sapiens

<400> 123
cgtggtgccc ctctatgacc tgctgctgga gatgctggac gcccaccgcc tacatgcgcc 60
cactagcc 68

<210> 124
<211> 20
<212> DNA
<213> Homo sapiens

<400> 124
tggtccatcg ccagttatca 20

<210> 125
<211> 23
<212> DNA
<213> Homo sapiens

<400> 125
tgttctagcg atcttgcttc aca 23

<210> 126
<211> 76
<212> DNA
<213> Homo sapiens

<400> 126
tggtccatcg ccagttatca catctgtatg cggaacctca aaagagtccc tggtgtgaag 60
caagatcgct agaaca 76

<210> 127
<211> 24
<212> DNA
<213> Homo sapiens

<400> 127
catccatgac aactttggta tcgt 24

<210> 128
<211> 21

<212> DNA
<213> Homo sapiens

<400> 128
cagtcttctg ggtggcagtg a 21

<210> 129
<211> 74
<212> DNA
<213> Homo sapiens

<400> 129
catccatgac aactttggta tcgtggaagg actcatgacc acagtccatg ccatcactgc 60
cacccagaag actg 74

<210> 130
<211> 23
<212> DNA
<213> Homo sapiens

<400> 130
caaaggagct cactgtggtg tct 23

<210> 131
<211> 26
<212> DNA
<213> Homo sapiens

<400> 131
gagtcagaat ggcttattca cagatg 26

<210> 132
<211> 75
<212> DNA
<213> Homo sapiens

<400> 132
caaaggagct cactgtggtg tctgtgttcc aaccactgaa tctggacccc atctgtgaat 60
aagccattct gactc 75

<210> 133
<211> 20
<212> DNA
<213> Homo sapiens

<400> 133
ccatctgcat ccatcttgtt 20

<210> 134
<211> 20
<212> DNA
<213> Homo sapiens

<400> 134
ggccaccagg gtattatctg 20

<210> 135
<211> 67
<212> DNA
<213> Homo sapiens

<400> 135
ccatctgcat ccatcttgtt tgggctcccc acccttgaga agtgcctcag ataataccct 60
ggtggcc 67

<210> 136
<211> 23
<212> DNA

<213> Homo sapiens

<400> 136
cgaaaagatg ctgaacagtg aca 23

<210> 137
<211> 20
<212> DNA
<213> Homo sapiens

<400> 137
tcaggaacag ccaccagtga 20

<210> 138
<211> 73
<212> DNA
<213> Homo sapiens

<400> 138
cgaaaagatg ctgaacagtg acaaatccaa ctgaccagaa gggaggagga agctcactgg 60
tggctgttcc tga 73

<210> 139
<211> 20
<212> DNA
<213> Homo sapiens

<400> 139
gagaccctgc tgtcccagaa 20

<210> 140
<211> 23
<212> DNA
<213> Homo sapiens

<400> 140
ggttgtagtc agcgaaggag atc 23

<210> 141
<211> 76
<212> DNA
<213> Homo sapiens

<400> 141
gagaccctgc tgtcccagaa ccagggaggc aagaccttca ttgtgggaga ccagatctcc 60
ttcgctgact acaacc 76

<210> 142
<211> 20
<212> DNA
<213> Homo sapiens

<400> 142
cccactcagt agccaagtca 20

<210> 143
<211> 20
<212> DNA
<213> Homo sapiens

<400> 143
cacgcaggtg gtatcagtct 20

<210> 144
<211> 73
<212> DNA
<213> Homo sapiens

<400> 144
cccactcagt agccaagtca caatgtttgg aaaacagccc gtttacttga gcaagactga 60
taccacctgc gtg 73

<210> 145
<211> 24
<212> DNA
<213> Homo sapiens

<400> 145
catcaaatgt cagccctgga gttc 24

<210> 146
<211> 26
<212> DNA
<213> Homo sapiens

<400> 146
ttcctgtagg tctttacccc gatagc 26

<210> 147
<211> 85
<212> DNA
<213> Homo sapiens

<400> 147
catcaaatgt cagccctgga gttccatgat accacacgaa cacagctttt tgccttcgag 60
ctatcggggt aaagacctac aggaa 85

<210> 148
<211> 24
<212> DNA
<213> Homo sapiens

<400> 148
tccaggatgt taggaactgt gaag 24

<210> 149
<211> 22
<212> DNA
<213> Homo sapiens

<400> 149
gcgtgtctgc gtagtagctg tt 22

<210> 150
<211> 73
<212> DNA
<213> Homo sapiens

<400> 150
tccaggatgt taggaactgt gaagatggaa gggcatgaaa ccagcgactg gaacagctac 60
tacgcagaca cgc 73

<210> 151
<211> 23
<212> DNA
<213> Homo sapiens

<400> 151
aacgactgct actccaagct caa 23

<210> 152
<211> 22
<212> DNA
<213> Homo sapiens

<400> 152

ggatttccat cttgctcacc tt 22

<210> 153
<211> 76
<212> DNA
<213> Homo sapiens

<400> 153
aacgactgct actccaagct caaggagctg gtgcccagca tcccccagaa caagaaggtg 60
agcaagatgg aaatcc 76

<210> 154
<211> 21
<212> DNA
<213> Homo sapiens

<400> 154
tccggagctg tgatctaagg a 21

<210> 155
<211> 20
<212> DNA
<213> Homo sapiens

<400> 155
cggacagagc gagctgactt 20

<210> 156
<211> 76
<212> DNA
<213> Homo sapiens

<400> 156
tccggagctg tgatctaagg aggctggaga tgtattgcgc acccctcaag cctgccaagt 60
cagctcgctc tgtccg 76

<210> 157
<211> 17
<212> DNA
<213> Homo sapiens

<400> 157
acgcaccggg tgtctga 17

<210> 158
<211> 24
<212> DNA
<213> Homo sapiens

<400> 158
tgccctttct tgatgatgat tatc 24

<210> 159
<211> 68
<212> DNA
<213> Homo sapiens

<400> 159
acgcaccggg tgtctgatcc caagttccac cccctccatt caaagataat catcatcaag 60
aaagggca 68

<210> 160
<211> 22
<212> DNA
<213> Homo sapiens

<400> 160
ccattcaccc tgtgtaacag ga 22

<210> 161
<211> 21
<212> DNA
<213> Homo sapiens

<400> 161
ccgaccctct aggttaaggc a 21

<210> 162
<211> 68
<212> DNA
<213> Homo sapiens

<400> 162
ccattcaccc tgtgtaacag gaccccaagg acctgcctcc ccggaagtgc cttaacctag 60
agggtcgg 68

<210> 163
<211> 20
<212> DNA
<213> Homo sapiens

<400> 163
cgtcaggacc caccatgtct 20

<210> 164
<211> 24
<212> DNA
<213> Homo sapiens

<400> 164
ggttaattgg tgacatcctc aaga 24

<210> 165
<211> 81
<212> DNA
<213> Homo sapiens

<400> 165
cgtcaggacc caccatgtct gccccatcac gcggccgaga catggcttgg ccacagctct 60
tgaggatgtc accaattaac c 81

<210> 166
<211> 23
<212> DNA
<213> Homo sapiens

<400> 166
caaacgctga catgtacggt cta 23

<210> 167
<211> 18
<212> DNA
<213> Homo sapiens

<400> 167
gctcgttggc gcactctt 18

<210> 168
<211> 88
<212> DNA
<213> Homo sapiens

<400> 168
caaacgctga catgtacggt ctatgccatt cctcccccgc atcacatcca ctggtattgg 60
cagttggagg aagagtgcgc caacgagc 88

<210> 169
<211> 25
<212> DNA
<213> Homo sapiens

<400> 169
gaggcaactg cttatggctt aatta 25

<210> 170
<211> 18
<212> DNA
<213> Homo sapiens

<400> 170
ggcactcggc ttgagcat 18

<210> 171
<211> 75
<212> DNA
<213> Homo sapiens

<400> 171
gaggcaactg cttatggctt aattaagtca gatgcggcca tgactgtcgc tgtaaagatg 60
ctcaagccga gtgcc 75

<210> 172
<211> 18
<212> DNA
<213> Homo sapiens

<400> 172
gtccccggga tggatgtt 18

<210> 173
<211> 25
<212> DNA
<213> Homo sapiens

<400> 173
gatcagtcaa gctgtctgac aattg 25

<210> 174
<211> 79
<212> DNA
<213> Homo sapiens

<400> 174
gtccccggga tggatgtttt gccaagtcat tgttggataa gcgagatggt agtacaattg 60
tcagacagct tgactgatc 79

<210> 175
<211> 21
<212> DNA
<213> Homo sapiens

<400> 175
cgaggattgg ttcttcagca a 21

<210> 176
<211> 22
<212> DNA
<213> Homo sapiens

<400> 176
actctgcacc agctcactgt tg 22

<210> 177
<211> 73

<212> DNA
<213> Homo sapiens

<400> 177
cgaggattgg ttcttcagca agacagagga actgaaccgc gaggtggcca ccaacagtga 60
gctggtgcag agt 73

<210> 178
<211> 20
<212> DNA
<213> Homo sapiens

<400> 178
tcagtggaga aggagttgga 20

<210> 179
<211> 20
<212> DNA
<213> Homo sapiens

<400> 179
tgccatatcc agaggaaaca 20

<210> 180
<211> 69
<212> DNA
<213> Homo sapiens

<400> 180
tcagtggaga aggagttgga ccagtcaaca tctctgttgt cacaagcagt gtttcctctg 60
gatatggca 69

<210> 181
<211> 26
<212> DNA
<213> Homo sapiens

<400> 181
gtacaagaga gaaccagact ccaatg 26

<210> 182
<211> 18
<212> DNA
<213> Homo sapiens

<400> 182
gtgtagcccg cggacact 18

<210> 183
<211> 87
<212> DNA
<213> Homo sapiens

<400> 183
gtacaagaga gaaccagact ccaatgtcat tgtggtggac tggctgtcac gggctcagga 60
gcattaccca gtgtccgcgg gctacac 87

<210> 184
<211> 22
<212> DNA
<213> Homo sapiens

<400> 184
gacatttcca gtcctgcagt ca 22

<210> 185
<211> 20
<212> DNA

<213> Homo sapiens

<400> 185
ctccgatcgc acacatttgt 20

<210> 186
<211> 86
<212> DNA
<213> Homo sapiens

<400> 186
gacatttcca gtcctgcagt caatgcctct ctgccccacc ctttgttcag tgtggctggt 60
gccacgacaa atgtgtgcga tcggag 86

<210> 187
<211> 24
<212> DNA
<213> Homo sapiens

<400> 187
gttttggagg aaatgtgttc ttca 24

<210> 188
<211> 26
<212> DNA
<213> Homo sapiens

<400> 188
ttctctaata cactgccgtc ttaagg 26

<210> 189
<211> 101
<212> DNA
<213> Homo sapiens

<400> 189
gttttggagg aaatgtgttc ttcagtgcac agaatgcagc aaaacagcca tctgataaat 60
gctctgcaag ccctccctta agacggcagt gtattagaga a 101

<210> 190
<211> 22
<212> DNA
<213> Homo sapiens

<400> 190
acgagaacga gggcatctat gt 22

<210> 191
<211> 22
<212> DNA
<213> Homo sapiens

<400> 191
gcatgtaggt gcttccaatc ac 22

<210> 192
<211> 75
<212> DNA
<213> Homo sapiens

<400> 192
acgagaacga gggcatctat gtgcaggatg tcaagaccgg aaaggtgcgc gctgtgattg 60
gaagcaccta catgc 75

<210> 193
<211> 21
<212> DNA
<213> Homo sapiens

<400> 193
tccctccact cggaaggact a 21

<210> 194
<211> 22
<212> DNA
<213> Homo sapiens

<400> 194
cggttgttgc tgatctgtct ca 22

<210> 195
<211> 84
<212> DNA
<213> Homo sapiens

<400> 195
tccctccact cggaaggact atcctgctgc caagagggtc aagttggaca gtgtcagagt 60
cctgagacag atcagcaaca accg 84

<210> 196
<211> 19
<212> DNA
<213> Homo sapiens

<400> 196
ttgttggtgt gccctggtg 19

<210> 197
<211> 21
<212> DNA
<213> Homo sapiens

<400> 197
tgggttctgt ccaaacactg g 21

<210> 198
<211> 67
<212> DNA
<213> Homo sapiens

<400> 198
ttgttggtgt gccctggtgc cgtggtggcg gtcactccct ctgctgccag tgtttggaca 60
gaaccca 67

<210> 199
<211> 20
<212> DNA
<213> Homo sapiens

<400> 199
actgaaggag acccttggag 20

<210> 200
<211> 20
<212> DNA
<213> Homo sapiens

<400> 200
taaataaccc tgcccacaca 20

<210> 201
<211> 62
<212> DNA
<213> Homo sapiens

<400> 201

actgaaggag acccttggag cctaggggca tcggcaggag agtgtgtggg cagggttatt 60
ta 62

<210> 202
<211> 28
<212> DNA
<213> Homo sapiens

<400> 202
agttactaaa aaataccacg aggtcctt 28

<210> 203
<211> 21
<212> DNA
<213> Homo sapiens

<400> 203
gtcggtgagt gatttgtgca a 21

<210> 204
<211> 79
<212> DNA
<213> Homo sapiens

<400> 204
agttactaaa aaataccacg aggtccttca gttgagacca aagaccggtg tcaggggatt 60
gcacaaatca ctcaccgac 79

<210> 205
<211> 20
<212> DNA
<213> Homo sapiens

<400> 205
gggagtttcc aagagatgga 20

<210> 206
<211> 20
<212> DNA
<213> Homo sapiens

<400> 206
cttcaaccac cttcccaaac 20

<210> 207
<211> 72
<212> DNA
<213> Homo sapiens

<400> 207
gggagtttcc aagagatgga ctagtgcttg gtcgggtctt ggggtctgga gcgtttggga 60
aggtggttga ag 72

<210> 208
<211> 23
<212> DNA
<213> Homo sapiens

<400> 208
aggtgtcatc catcaacgtc tct 23

<210> 209
<211> 20
<212> DNA
<213> Homo sapiens

<400> 209
tcccgatcac aatgcacatg 20

<210> 210
<211> 90
<212> DNA
<213> Homo sapiens

<400> 210
aggtgtcatc catcaacgtc tctgtgaacg cagtgcagac tgtggtccgc cagggtgaga 60
acatcaccct catgtgcatt gtgatcggga 90

<210> 211
<211> 24
<212> DNA
<213> Homo sapiens

<400> 211
agagccagtt gctgtagaac tcaa 24

<210> 212
<211> 21
<212> DNA
<213> Homo sapiens

<400> 212
ctgggcctac acagtccttc a 21

<210> 213
<211> 74
<212> DNA
<213> Homo sapiens

<400> 213
agagccagtt gctgtagaac tcaaatctct gctgggcaag gatgttctgt tcttgaagga 60
ctgtgtaggc ccag 74

<210> 214
<211> 26
<212> DNA
<213> Homo sapiens

<400> 214
gaaatgactg catcgttgat aaaatc 26

<210> 215
<211> 19
<212> DNA
<213> Homo sapiens

<400> 215
tgccagcctg acagcactt 19

<210> 216
<211> 78
<212> DNA
<213> Homo sapiens

<400> 216
gaaatgactg catcgttgat aaaatccgca gaaaaaactg cccagcatgt cgccttagaa 60
agtgctgtca ggctggca 78

<210> 217
<211> 20
<212> DNA
<213> Homo sapiens

<400> 217
gatcaacggc tacatccaga 20

<210> 218
<211> 20
<212> DNA
<213> Homo sapiens

<400> 218
tgaactgtga ggccagagac 20

<210> 219
<211> 68
<212> DNA
<213> Homo sapiens

<400> 219
gatcaacggc tacatccaga agatcaagtc gggagaggag gactttgagt ctctggcctc 60
acagttca 68

<210> 220
<211> 19
<212> DNA
<213> Homo sapiens

<400> 220
gtggatgtgc cctgaagga 19

<210> 221
<211> 20
<212> DNA
<213> Homo sapiens

<400> 221
ctgcggatcc agggtaagaa 20

<210> 222
<211> 70
<212> DNA
<213> Homo sapiens

<400> 222
gtggatgtgc cctgaaggac aagccaggcg tctacacgag agtctcacac ttcttaccct 60
ggatccgcag 70

<210> 223
<211> 27
<212> DNA
<213> Homo sapiens

<400> 223
tggacttcta gtgatgagaa agattga 27

<210> 224
<211> 22
<212> DNA
<213> Homo sapiens

<400> 224
cactgcgaga tcaccacagg ta 22

<210> 225
<211> 84
<212> DNA
<213> Homo sapiens

<400> 225
tggacttcta gtgatgagaa agattgagaa tgttcccaca ggccccaaca ataagcccaa 60
gctacctgtg gtgatctcgc agtg 84

<210> 226

<211> 25
<212> DNA
<213> Homo sapiens

<400> 226
tggctaagtg aagatgacaa tcatg 25

<210> 227
<211> 25
<212> DNA
<213> Homo sapiens

<400> 227
tgcacatatc attacaccag ttcgt 25

<210> 228
<211> 81
<212> DNA
<213> Homo sapiens

<400> 228
tggctaagtg aagatgacaa tcatgttgca gcaattcact gtaaagctgg aaagggacga 60
actggtgtaa tgatatgtgc a 81

<210> 229
<211> 23
<212> DNA
<213> Homo sapiens

<400> 229
tctgcagagt tggaagcact cta 23

<210> 230
<211> 21
<212> DNA
<213> Homo sapiens

<400> 230
gccgaggctt ttctaccaga a 21

<210> 231
<211> 79
<212> DNA
<213> Homo sapiens

<400> 231
tctgcagagt tggaagcact ctatggtgac atcgatgctg tggagctgta tcctgccctt 60
ctggtagaaa agcctcggc 79

<210> 232
<211> 24
<212> DNA
<213> Homo sapiens

<400> 232
acgacacgta tgccgtacag tact 24

<210> 233
<211> 18
<212> DNA
<213> Homo sapiens

<400> 233
ccgggaaaac acgaagga 18

<210> 234
<211> 86
<212> DNA

<213> Homo sapiens

<400> 234
acgacacgta tgccgtacag tactcctgcc gcctcctgaa cctcgatggc acctgtgctg 60
acagctactc cttcgtgttt tcccgg 86

<210> 235
<211> 19
<212> DNA
<213> Homo sapiens

<400> 235
ctgccgggat ggcttctat 19

<210> 236
<211> 22
<212> DNA
<213> Homo sapiens

<400> 236
ccaggttctg gaaactgtgg at 22

<210> 237
<211> 68
<212> DNA
<213> Homo sapiens

<400> 237
ctgccgggat ggcttctatg aggctgagct ctgcccggac cgctgcatcc acagtttcca 60
gaacctgg 68

<210> 238
<211> 20
<212> DNA
<213> Homo sapiens

<400> 238
ccacaagctg aaggcagaca 20

<210> 239
<211> 21
<212> DNA
<213> Homo sapiens

<400> 239
gcgtgcttcc ttggtcttag a 21

<210> 240
<211> 85
<212> DNA
<213> Homo sapiens

<400> 240
ccacaagctg aaggcagaca aggcccgcaa gaagctcctg gctgaccagg ctgaggcccg 60
caggtctaag accaaggaag cacgc 85

<210> 241
<211> 24
<212> DNA
<213> Homo sapiens

<400> 241
ccattctatc atcaacgggt acaa 24

<210> 242
<211> 23
<212> DNA
<213> Homo sapiens

<400> 242
tcagcaagtg ggaaggtgta atc 23

<210> 243
<211> 75
<212> DNA
<213> Homo sapiens

<400> 243
ccattctatc atcaacgggt acaaacgagt cctggccttg tctgtggaga cggattacac 60
cttcccactt gctga 75

<210> 244
<211> 20
<212> DNA
<213> Homo sapiens

<400> 244
tatcgaggca ggtcatacca 20

<210> 245
<211> 20
<212> DNA
<213> Homo sapiens

<400> 245
taacgcttgg catcatcatt 20

<210> 246
<211> 74
<212> DNA
<213> Homo sapiens

<400> 246
tatcgaggca ggtcatacca tgaccggaag tcaaaagttg acctggatag gctcaatgat 60
gatgccaagc gtta 74

<210> 247
<211> 19
<212> DNA
<213> Homo sapiens

<400> 247
ccgcaacgtg gttttctca 19

<210> 248
<211> 21
<212> DNA
<213> Homo sapiens

<400> 248
tgctgggttt ctcctcctgt t 21

<210> 249
<211> 81
<212> DNA
<213> Homo sapiens

<400> 249
ccgcaacgtg gttttctcac cctatggggt ggcctcggtg ttggccatgc tccagctgac 60
aacaggagga gaaacccagc a 81

<210> 250
<211> 25
<212> DNA
<213> Homo sapiens

<400> 250
tcaagaccat catcactttc attgt 25

<210> 251
<211> 27
<212> DNA
<213> Homo sapiens

<400> 251
ggatcaggaa gtacacggag tataact 27

<210> 252
<211> 96
<212> DNA
<213> Homo sapiens

<400> 252
tcaagaccat catcactttc attgtctcgg acgtgcgggg cctgggcctc ccggtccgca 60
agcagttcca gttatactcc gtgtacttcc tgatcc 96

<210> 253
<211> 19
<212> DNA
<213> Homo sapiens

<400> 253
gcccgaaacg ccgaatata 19

<210> 254
<211> 23
<212> DNA
<213> Homo sapiens

<400> 254
cgtggctctc ttatcctcat gat 23

<210> 255
<211> 65
<212> DNA
<213> Homo sapiens

<400> 255
gcccgaaacg ccgaatataa tcccaagcgg tttgctgcgg taatcatgag gataagagag 60
ccacg 65

<210> 256
<211> 19
<212> DNA
<213> Homo sapiens

<400> 256
gccctcccag tgtgcaaat 19

<210> 257
<211> 25
<212> DNA
<213> Homo sapiens

<400> 257
cgtcgatggt attaggatag aagca 25

<210> 258
<211> 86
<212> DNA
<213> Homo sapiens

<400> 258
gccctcccag tgtgcaaata agggctgctg tttcgacgac accgttcgtg ggtcccctg 60

gtgcttctat cctaatacca tcgacg 86

<210> 259
<211> 27
<212> DNA
<213> Homo sapiens

<400> 259
caagctagat cagcattctc taacttg 27

<210> 260
<211> 25
<212> DNA
<213> Homo sapiens

<400> 260
cacatgactg ttatcgccat ctact 25

<210> 261
<211> 99
<212> DNA
<213> Homo sapiens

<400> 261
caagctagat cagcattctc taacttgttt ggtggagaac cattgtcata tacccggttc 60
agcctggctc ggcaagtaga tggcgataac agtcatgtg 99

<210> 262
<211> 22
<212> DNA
<213> Homo sapiens

<400> 262
cacaggaaca acagcatctt tc 22

<210> 263
<211> 20
<212> DNA
<213> Homo sapiens

<400> 263
agataagccc ctgggatcca 20

<210> 264
<211> 75
<212> DNA
<213> Homo sapiens

<400> 264
cacaggaaca acagcatctt tcaccaagat gggtggcacc aaccttgctg ggacttggat 60
cccaggggct tatct 75

<210> 265
<211> 21
<212> DNA
<213> Homo sapiens

<400> 265
ggattgctca acaaccatgc t 21

<210> 266
<211> 24
<212> DNA
<213> Homo sapiens

<400> 266
ggcattaaca cttttggacg ataa 24

<210> 267
<211> 91
<212> DNA
<213> Homo sapiens

<400> 267
ggattgctca acaaccatgc tgggcatctg gaccctccta cctctggttc ttacgtctgt 60
tgctagatta tcgtccaaaa gtgttaatgc c 91

<210> 268
<211> 24
<212> DNA
<213> Homo sapiens

<400> 268
gcactttggg attctttcca ttat 24

<210> 269
<211> 24
<212> DNA
<213> Homo sapiens

<400> 269
gcatgtaaga agaccctcac tgaa 24

<210> 270
<211> 80
<212> DNA
<213> Homo sapiens

<400> 270
gcactttggg attctttcca ttatgattct ttgttacagg caccgagaat gttgtattca 60
gtgagggtct tcttacatgc 80

<210> 271
<211> 20
<212> DNA
<213> Homo sapiens

<400> 271
aatccaaggg ggagagtgat 20

<210> 272
<211> 20
<212> DNA
<213> Homo sapiens

<400> 272
gtacagattt tgcccgagga 20

<210> 273
<211> 72
<212> DNA
<213> Homo sapiens

<400> 273
aatccaaggg ggagagtgat gacttccata tggactttga ctcagctgtg gctcctcggg 60
caaaatctgt ac 72

<210> 274
<211> 21
<212> DNA
<213> Homo sapiens

<400> 274
tgtggacatc ttcccctcag a 21

<210> 275

<211> 18
<212> DNA
<213> Homo sapiens

<400> 275
ctagcccgac cggttcgt 18

<210> 276
<211> 66
<212> DNA
<213> Homo sapiens

<400> 276
tgtggacatc ttcccctcag acttccctac tgagccacct tctctgccac gaaccggtcg 60
ggctag 66

<210> 277
<211> 20
<212> DNA
<213> Homo sapiens

<400> 277
ctttgaaccc ttgcttgcaa 20

<210> 278
<211> 18
<212> DNA
<213> Homo sapiens

<400> 278
cccgggacaa agcaaatg 18

<210> 279
<211> 68
<212> DNA
<213> Homo sapiens

<400> 279
ctttgaaccc ttgcttgcaa taggtgtgcg tcagaagcac ccaggacttc catttgcttt 60
gtcccggg 68

<210> 280
<211> 18
<212> DNA
<213> Homo sapiens

<400> 280
gcctcggtgt gcctttca 18

<210> 281
<211> 19
<212> DNA
<213> Homo sapiens

<400> 281
cgtgatgtgc gcaatcatg 19

<210> 282
<211> 65
<212> DNA
<213> Homo sapiens

<400> 282
gcctcggtgt gcctttcaac atcgccagct acgccctgct cacgtacatg attgcgcaca 60
tcacg 65

<210> 283
<211> 20

<212> DNA
<213> Homo sapiens

<400> 283
ctgctgtctt gggtgcattg 20

<210> 284
<211> 18
<212> DNA
<213> Homo sapiens

<400> 284
gcagcctggg accacttg 18

<210> 285
<211> 71
<212> DNA
<213> Homo sapiens

<400> 285
ctgctgtctt gggtgcattg gagccttgcc ttgctgctct acctccacca tgccaagtgg 60
tcccaggctg c 71

<210> 286
<211> 1947
<212> DNA
<213> Homo sapiens

<400> 286
ttttccccag atatggggtt ctattcagcc atagataatc tagacagagg atttcagaat 60
gaaaggaaaa atgtgtggag attagtccta gttcattctg agggccgact aagtggctca 120
gccagcttct tactccatct gcagttcata ctgccaaaga gctcccactt ccaaatcccc 180
agtgacttta tggagaagat tctgcattaa attgtctttc gaatgatggg gaagcaaggc 240
ataatatgcg atgatgagga gaaagtagac cagtgaggtg attgcaagac taacaaggag 300
actcaatggg aagtttttct ttcttttaga tattgctttt gaagtagatg gtaaaatttt 360
tgtcatcctt cttgtatttt ttgtacccca agttacaatt tttcttcttc cttgtaaata 420
atttaaacag tatttatttt tgtaaggcat aactagaaac taaaatatat tctaaaaaat 480
tcattattct gaacaaagtg atcaaattag aatacatatt tttcaacagt ggtagagctt 540
ttaatatatg tttattgaaa gttatctata atacttgcac cagtgttgaa aaaagttaac 600
atgtaggcaa gagcaatatg tttgtctcaa ggatttttcc atggtttcct cagtgatggt 660
gtcctggaat tattcaggtg gtgaccatca ctggtctaag tttgtgtgca gggttttcag 720
acgtgttttt gtgaaacttg gtagaaccat ggctaataaa gaggacagtg ttgtcagggt 780
ccatctgccc tccatagaaa aatgtctctg gctcataaaa tgagactccc tcagggacta 840
aatatgaact gacagcagta actctgatac agaataatct aaattgcatc aaatggcctt 900
aattcagagt ttgttaggct tatcagtatg ttgcttttaa ttggggtggg aaagtagagg 960
gagagaaagc aagacattta ttaagcacct cgtatgtgcc aggcactatg ctaagcactt 1020
tacataagtt aggattaatc cctgcaagaa tcctataaag aatgttacta gcatttacac 1080
ttcccaaatg aaggtaccaa agctcaaacg caatgttgtg aagctgtttc cttcagattt 1140
aggttatgtg ggatgatgtg ggattgaaga ggaaagaaag gtgggattat cccccctagga 1200
agactttcag gcctgacttc ataggaattc atccatctta tcatgtggag tttatctcac 1260
cctgctgttg caggatgcta tttgcatgtg tccccaggtg atgtttttc tttggggagt 1320
aggggtttgg cttcctcatt catccctctt gctaaaagag gagatagttg atgttgcatc 1380
taaagatgct ataagacaat gaaagtttga tgttgtacat acctacaagt accatttttg 1440
tgcatgatta cactccactg acatcttcca agtactgcat gtgattgaat aagaaacaag 1500
aaagtgacca caccaaagcc tccctggctg gtgtacaggg atcaggtcca cagtggtaca 1560
gattcaacca ccacccaggg agtgcttgca gactctgcat agatgttgct gcatgcgtcc 1620
catgtgcctg tcagaatggc agtgtttaat tctcttgaaa gaaagttatt tgctcactat 1680
ccccagcctc aaggagccaa ggaagagtca ttcacatgga aggtccgggt ctggtcagcc 1740
actctgactt ttctaccaca ttaaattctc cattacatct cactattggt aatggcttaa 1800
gtgtaaagag ccatgatgtg tatattaagc tatgtgccac atatttattt ttagactctc 1860
cacagcattc atgtcaatat gggattaatg cctaaacttt gtaaatattg tacagtttgt 1920
aaatcaatga ataaaggttt tgagtgt 1947

<210> 287
<211> 1311
<212> DNA
<213> Homo sapiens

<400> 287
tagtcgggcg gggttgtgag acgccgcgct cagcttccat cgctgggcgg tcaacaagtg 60
cgggcctggc tcagcgcggg ggggcgcgga gaccgcgagg cgaccgggag cggctgggtt 120
cccggctgcg cgcccttcgg ccaggccggg agccgcgcca gtcggagccc ccggcccagc 180
gtggtccgcc tccctctcgg cgtccacctg cccggagtac tgccagcggg catgaccgac 240
ccaccagggg cgccgccgcc ggcgctcgca ggccgcggat gaagaagaaa acccggcgcc 300
gctcgacccg gagcgaggag ttgacccgga gcgaggagtt gaccctgagt gaggaagcga 360
cctggagtga agaggcgacc cagagtgagg aggcgaccca gggcgaagag atgaatcgga 420
gccaggaggt gacccgggac gaggagtcga cccggagcga ggaggtgacc agggaggaaa 480
tggcggcagc tgggctcacc gtgactgtca cccacagcaa tgagaagcac gaccttcatg 540
ttacctccca gcagggcagc agtgaaccag ttgtccaaga cctggcccag gttgttgaag 600
aggtcatagg ggttccacag tcttttcaga aactcatatt taagggaaaa tctctgaagg 660
aaatggaaac accgttgtca gcacttggaa tacaagatgg ttgccgggtc atgttaattg 720
ggaaaaagaa cagtccacag gaagaggttg aactaaagaa gttgaaacat ttggagaagt 780
ctgtggagaa gatagctgac cagctggaag agttgaataa agagcttact ggaatccagc 840
agggttttct gcccaaggat ttgcaagctg aagctctctg caaacttgat aggagagtaa 900
aagccacaat agagcagttt atgaagatct tggaggagat tgacacactg atcctgccag 960
aaaatttcaa agacagtaga ttgaaaagga aaggcttggt aaaaaaggtt caggcattcc 1020
tagccgagtg tgacacagtg gagcagaaca tctgccagga gactgagcgg ctgcagtcta 1080
caaactttgc cctggccgag tgaggtgtag cagaaaaagg ctgtgctgcc ctgaagaatg 1140
gcgccaccag ctctgccgtc tctggatcgg aatttacctg atttcttcag ggctgctggg 1200
ggcaactggc catttgccaa ttttcctact ctcacactgg ttctcaatga aaaatagtgt 1260
ctttgtgatt tgagtaaagc tcctattctg tttttcacaa aaaaaaaaaa a 1311

<210> 288
<211> 582
<212> DNA
<213> Homo sapiens

<400> 288
atggcccgcg cacgccagga gggcagctcc ccggagcccg tagagggcct ggcccgcgac 60
ggcccgcgcc ccttcccgct cggccgcctg gtgccctcgg cagtgtcctg cggcctctgc 120
gagcccggcc tggctgccgc ccccgccgcc cccaccctgc tgcccgctgc ctacctctgc 180
gcccccaccg ccccacccgc cgtcaccgcc gccctggggg gttcccgctg gcctgggggt 240
ccccgcagcc ggccccgagg cccgcgcccg gacggtcctc agccctcgct ctcgctggcg 300
gagcagcacc tggagtcgcc cgtgcccagc gccccggggg ctctggcggg cggtcccacc 360
caggcggccc cgggagtccg cggggaggag gaacagtggg cccgggagat cggggcccag 420
ctgcggcgga tggcggacga cctcaacgca cagtacgagc ggcggagaca agaggagcag 480
cagcggcacc gcccctcacc ctggagggtc ctgtacaatc tcatcatggg actcctgccc 540
ttacccaggg gccacagagc cccgagatg gagcccaatt ag 582

<210> 289
<211> 6030
<212> DNA
<213> Homo sapiens

<400> 289
gttggccccc gttacttttc ctctgggaaa tatggcgcac gctgggagaa cagggtacga 60
taaccgggag atagtgatga agtacatcca ttataagctg tcgcagaggg gctacgagtg 120
ggatgcggga gatgtgggcg ccgcgccccc gggggccgcc cccgcgccgg gcatcttctc 180
ctcgcagccc gggcacacgc cccatacagc cgcatcccgg gacccggtcg ccaggacctc 240
gccgctgcag accccggctg cccccggcgc cgccgcgggg cctgcgctca gcccggtgcc 300
acctgtggtc cacctgaccc tccgccaggc cggcgacgac ttctcccgcc gctaccgccg 360
cgacttcgcc gagatgtcca ggcagctgca cctgacgccc ttcaccgcgc ggggacgctt 420
tgccacggtg gtggaggagc tcttcaggga cggggtgaac tgggggagga ttgtggcctt 480
ctttgagttc ggtggggtca tgtgtgtgga gagcgtcaac cgggagatgt cgcccctggt 540
ggacaacatc gccctgtgga tgactgagta cctgaaccgg cacctgcaca cctggatcca 600
ggataacgga ggctgggatg cctttgtgga actgtacggc cccagcatgc ggcctctgtt 660
tgatttctcc tggctgtctc tgaagactct gctcagtttg gccctggtgg gagcttgcat 720
caccctgggt gcctatctgg gccacaagtg aagtcaacat gcctgcccca aacaaatatg 780
caaaaggttc actaaagcag tagaaataat atgcattgtc agtgatgttc catgaaacaa 840
agctgcaggc tgtttaagaa aaaataacac acatataaac atcacacaca cagacagaca 900
cacacacaca caacaattaa cagtcttcag gcaaaacgtc gaatcagcta tttactgcca 960
aagggaaata tcatttattt tttacattat taagaaaaaa agatttattt atttaagaca 1020
gtcccatcaa aactcctgtc tttggaaatc cgaccactaa ttgccaagca ccgcttcgtg 1080
tggctccacc tggatgttct gtgcctgtaa acatagattc gctttccatg ttgttggccg 1140
gatcaccatc tgaagagcag acggatggaa aaaggacctg atcattgggg aagctggctt 1200
tctggctgct ggaggctggg gagaaggtgt tcattcactt gcatttcttt gccctggggg 1260

ctgtgatatt aacagaggga gggttcctgt ggggggaagt ccatgcctcc ctggcctgaa 1320
gaagagactc tttgcatatg actcacatga tgcatacctg gtgggaggaa aagagttggg 1380
aacttcagat ggacctagta cccactgaga tttccacgcc gaaggacagc gatgggaaaa 1440
atgcccttaa atcataggaa agtatttttt taagctacca attgtgccga gaaaagcatt 1500
ttagcaattt atacaatatc atccagtacc ttaagccctg attgtgtata ttcatatatt 1560
ttggatacgc acccccccaac tcccaatact ggctctgtct gagtaagaaa cagaatcctc 1620
tggaacttga ggaagtgaac atttcggtga cttccgcatc aggaaggcta gagttaccca 1680
gagcatcagg ccgccacaag tgcctgcttt taggagaccg aagtccgcag aacctgcctg 1740
tgtcccagct tggaggcctg gtcctggaac tgagccgggg ccctcactgg cctcctccag 1800
ggatgatcaa cagggcagtg tggtctccga atgtctggaa gctgatggag ctcagaattc 1860
cactgtcaag aaagagcagt agaggggtgt ggctgggcct gtcaccctgg ggccctccag 1920
gtaggcccgt tttcacgtgg agcatgggag ccacgaccct tcttaagaca tgtatcactg 1980
tagagggaag gaacagaggc cctgggccct tcctatcaga aggacatggt gaaggctggg 2040
aacgtgagga gaggcaatgg ccacggccca ttttggctgt agcacatggc acgttggctg 2100
tgtggccttg gcccacctgt gagtttaaag caaggcttta aatgactttg gagagggtca 2160
caaatcctaa aagaagcatt gaagtgaggt gtcatggatt aattgacccc tgtctatgga 2220
attacatgta aaacattatc ttgtcactgt agtttggttt tatttgaaaa cctgacaaaa 2280
aaaaagttcc aggtgtggaa tatggggtt atctgtacat cctggggcat taaaaaaaaa 2340
atcaatggtg gggaactata aagaagtaac aaaagaagtg acatcttcag caaataaact 2400
aggaaatttt tttttcttcc agtttagaat cagccttgaa acattgatgg aataactctg 2460
tggcattatt gcattatata ccatttatct gtattaactt tggaatgtac tctgttcaat 2520
gtttaatgct gtggttgata tttcgaaagc tgctttaaaa aaatacatgc atctcagcgt 2580
tttttgttt ttaattgtat ttagttatgg cctatacact atttgtgagc aaaggtgatc 2640
gttttctgtt tgagattttt atctcttgat tcttcaaaag cattctgaga aggtgagata 2700
agccctgagt ctcagctacc taagaaaaac ctggatgtca ctggccactg aggagctttg 2760
tttcaaccaa gtcatgtgca tttccacgtc aacagaattg tttattgtga cagttatatc 2820
tgttgtccct ttgaccttgt ttcttgaagg tttcctcgtc cctgggcaat tccgcattta 2880
attcatggta ttcaggatta catgcatgtt tggttaaacc catgagattc attcagttaa 2940
aaatccagat ggcaaatgac cagcagattc aaatctatgg tggtttgacc tttagagagt 3000
tgctttacgt ggcctgtttc aacacagacc cacccagagc cctcctgccc tccttccgcg 3060
ggggctttct catggctgtc cttcagggtc ttcctgaaat gcagtggtgc ttacgctcca 3120
ccaagaaagc aggaaacctg tggtatgaag ccagacctcc ccggcgggcc tcagggaaca 3180
gaatgatcag acctttgaat gattctaatt tttaagcaaa atattatttt atgaaaggtt 3240
tacattgtca aagtgatgaa tatggaatat ccaatcctgt gctgctatcc tgccaaaatc 3300
attttaatgg agtcagtttg cagtatgctc cacgtggtaa gatcctccaa gctgctttag 3360
aagtaacaat gaagaacgtg gacgctttta atataaagcc tgttttgtct tctgttgttg 3420
ttcaaacggg attcacagag tatttgaaaa atgtatatat attaagaggt cacgggggct 3480
aattgctggc tggctgcctt ttgctgtggg gttttgttac ctggttttaa taacagtaaa 3540
tgtgcccagc ctcttggccc cagaactgta cagtattgtg gctgcacttg ctctaagagt 3600
agttgatgtt gcattttcct tattgttaaa aacatgttag aagcaatgaa tgtatataaa 3660
agcctcaact agtcattttt ttctcctctt ctttttttc attatatcta attattttgc 3720
agttgggcaa cagagaacca tccctatttt gtattgaaga gggattcaca tctgcatctt 3780
aactgctctt tatgaatgaa aaaacagtcc tctgtatgta ctcctcttta cactggccag 3840
ggtcagagtt aaatagagta tatgcacttt ccaaattggg gacaagggct ctaaaaaaag 3900
ccccaaaagg agaagaacat ctgagaacct cctcggccct cccagtccct cgctgcacaa 3960
atactccgca agagaggcca gaatgacagc tgacagggtc tatggccatc gggtcgtctc 4020
cgaagatttg gcaggggcag aaaactctgg caggcttaag atttggaata aagtcacaga 4080
atcaaggaag cacctcaatt tagttcaaac aagacgccaa cattctctcc acagctcact 4140
tacctctctg tgttcagatg tggccttcca tttatatgtg atctttgttt tattagtaaa 4200
tgcttatcat ctaaagatgt agctctggcc cagtgggaaa aattaggaag tgattataaa 4260
tcgagaggag ttataataat caagattaaa tgtaaataat cagggcaatc ccaacacatg 4320
tctagctttc acctccagga tctattgagt gaacagaatt gcaaatagtc tctatttgta 4380
attgaactta tcctaaaaca aatagtttat aaatgtgaac ttaaactcta attaattcca 4440
actgtacttt taaggcagtg gctgttttta gactttctta tcacttatag ttagtaatgt 4500
acacctactc tatcagagaa aaacaggaaa ggctcgaaat acaagccatt ctaaggaaat 4560
tagggagtca gttgaaattc tattctgatc ttattctgtg gtgtcttttg cagcccagac 4620
aaatgtggtt acacactttt taagaaatac aattctacat tgtcaagctt atgaaggttc 4680
caatcagatc tttattgtta ttcaatttgg atctttcagg gatttttttt ttaaattatt 4740
atgggacaaa ggacatttgt tggaggggtg ggagggagga acaattttta aatataaaac 4800
attcccaagt ttggatcagg gagttggaag ttttcagaat aaccagaact aagggtatga 4860
aggacctgta ttggggtcga tgtgatgcct ctgcgaagaa ccttgtgtga caaatgagaa 4920
acattttgaa gtttgtggta cgacctttag attccagaga catcagcatg gctcaaagtg 4980
cagctccgtt tggcagtgca atggtataaa tttcaagctg gatatgtcta atgggtattt 5040
aaacaataaa tgtgcagttt taactaacag gatatttaat gacaaccttc tggttggtag 5100
ggacatctgt ttctaaatgt ttattatgta caatacagaa aaaaatttta taaaattaag 5160
caatgtgaaa ctgaattgga gagtgataat acaagtcctt tagtcttacc cagtgaatca 5220
ttctgttcca tgtctttgga caaccatgac cttggacaat catgaaatat gcatctcact 5280
ggatgcaaag aaaatcagat ggagcatgaa tggtactgta ccggttcatc tggactgccc 5340

cagaaaaata acttcaagca aacatcctat caacaacaag gttgttctgc ataccaagct 5400
gagcacagaa gatgggaaca ctggtggagg atggaaaggc tcgctcaatc aagaaaattc 5460
tgagactatt aataaataag actgtagtgt agatactgag taaatccatg cacctaaacc 5520
ttttggaaaa tctgccgtgg gccctccaga tagctcattt cattaagttt ttccctccaa 5580
ggtagaattt gcaagagtga cagtggattg catttctttt ggggaagctt tcttttggtg 5640
gttttgttta ttataccttc ttaagttttc aaccaaggtt tgcttttgtt ttgagttact 5700
ggggttattt ttgttttaaa taaaaataag tgtacaataa gtgtttttgt attgaaagct 5760
tttgttatca agattttcat acttttacct tccatggctc tttttaagat tgatactttt 5820
aagaggtggc tgatattctg caacactgta cacataaaaa atacggtaag gatactttac 5880
atggttaagg taaagtaagt ctccagttgg ccaccattag ctataatggc actttgtttg 5940
tgttgttgga aaaagtcaca ttgccattaa actttccttg tctgtctagt taatattgtg 6000
aagaaaaata aagtacagtg tgagatactg 6030

<210> 290
<211> 10987
<212> DNA
<213> Homo sapiens

<400> 290
ggtggcgcga gcttctgaaa ctaggcggca gaggcggagc cgctgtggca ctgctgcgcc 60
tctgctgcgc ctcgggtgtc ttttgcggcg gtgggtcgcc gccgggagaa gcgtgagggg 120
acagatttgt gaccggcgcg gtttttgtca gcttactccg gccaaaaaag aactgcacct 180
ctggagcgga cttatttacc aagcattgga ggaatatcgt aggtaaaaat gcctattgga 240
tccaaagaga ggccaacatt ttttgaaatt tttaagacac gctgcaacaa agcagattta 300
ggaccaataa gtcttaattg gtttgaagaa ctttcttcag aagctccacc ctataattct 360
gaacctgcag aagaatctga acataaaaac aacaattacg aaccaaacct atttaaaact 420
ccacaaagga aaccatctta taatcagctg gcttcaactc caataatatt caaagagcaa 480
gggctgactc tgccgctgta ccaatctcct gtaaaagaat tagataaatt caaattagac 540
ttaggaagga atgttcccaa tagtagacat aaaagtcttc gcacagtgaa aactaaaatg 600
gatcaagcag atgatgtttc ctgtccactt ctaaattctt gtcttagtga aagtcctgtt 660
gttctacaat gtacacatgt aacaccacaa agagataagt cagtggtatg tgggagtttg 720
tttcatacac caaagtttgt gaagggtcgt cagacaccaa aacatatttc tgaaagtcta 780
ggagctgagg tggatcctga tatgtcttgg tcaagttctt tagctacacc acccaccctt 840
agttctactg tgctcatagt cagaaatgaa gaagcatctg aaactgtatt tcctcatgat 900
actactgcta atgtgaaaag ctatttttcc aatcatgatg aaagtctgaa gaaaaatgat 960
agatttatcg cttctgtgac agacagtgaa aacacaaatc aaagagaagc tgcaagtcat 1020
ggatttggaa aaacatcagg gaattcattt aaagtaaata gctgcaaaga ccacattgga 1080
aagtcaatgc caaatgtcct agaagatgaa gtatatgaaa cagttgtaga tacctctgaa 1140
gaagatagtt tttcattatg tttttctaaa tgtagaacaa aaaatctaca aaaagtaaga 1200
actagcaaga ctaggaaaaa aattttccat gaagcaaacg ctgatgaatg tgaaaaatct 1260
aaaaaccaag tgaaagaaaa atactcattt gtatctgaag tggaaccaaa tgatactgat 1320
ccattagatt caaatgtagc acatcagaag ccctttgaga gtggaagtga caaaatctcc 1380
aaggaagttg taccgtcttt ggcctgtgaa tggtctcaac taacccttc aggtctaaat 1440
ggagcccaga tggagaaaat accctattg catatttctt catgtgacca aaatatttca 1500
gaaaaagacc tattagacac agagaacaaa agaaagaaag attttcttac ttcagagaat 1560
tctttgccac gtatttctag cctaccaaaa tcagagaagc cattaaatga ggaaacagtg 1620
gtaaataaga gagatgaaga gcagcatctt gaatctcata cagactgcat tcttgcagta 1680
aagcaggcaa tatctggaac ttctccagtg gcttcttcat ttcagggtat caaaaagtct 1740
atattcagaa taagagaatc acctaaagag actttcaatg caagttttc aggtcatatg 1800
actgatccaa actttaaaaa agaaactgaa gcctctgaaa gtggactgga aatacatact 1860
gtttgctcac agaaggagga ctccttatgt ccaaatttaa ttgataatgg aagctggcca 1920
gccaccacca cacagaattc tgtagctttg aagaatgcag gtttaatatc cactttgaaa 1980
aagaaaacaa ataagtttat ttatgctata catgatgaaa cattttataa aggaaaaaaa 2040
ataccgaaag accaaaaatc agaactaatt aactgttcag cccagtttga agcaaatgct 2100
tttgaagcac cacttacatt tgcaaatgct gattcaggtt tattgcattc ttctgtgaaa 2160
agaagctgtt cacagaatga ttctgaagaa ccaactttgt ccttaactag ctcttttggg 2220
acaattctga ggaaatgttc tagaaatgaa acatgttcta ataatacagt aatctctcag 2280
gatcttgatt ataaagaagc aaaatgtaat aaggaaaaac tacagttatt tattacccca 2340
gaagctgatt ctctgtcatg cctgcaggaa ggacagtgtg aaaatgatcc aaaaagcaaa 2400
aaagtttcag atataaaaga agaggtcttg gctgcagcat gtcacccagt acaacattca 2460
aaagtggaat acagtgatac tgactttcaa tcccagaaaa gtcttttata tgatcatgaa 2520
aatgccagca ctcttatttt aactcctact tccaaggatg ttctgtcaaa cctagtcatg 2580
atttctagag gcaaagaatc atacaaaatg tcagacaagc tcaaaggtaa caattatgaa 2640
tctgatgttg aattaaccaa aaatattccc atggaaaaga atcaagatgt atgtgcttta 2700
aatgaaaatt ataaaaacgt tgagctgttg ccacctgaaa aatacatgag agtagcatca 2760
ccttcaagaa aggtacaatt caaccaaaac acaaatctaa gagtaatcca aaaaaatcaa 2820

gaagaaacta cttcaatttc aaaaataact gtcaatccag actctgaaga acttttctca 2880
gacaatgaga ataattttgt cttccaagta gctaatgaaa ggaataatct tgctttagga 2940
aatactaagg aacttcatga aacagacttg acttgtgtaa acgaacccat tttcaagaac 3000
tctaccatgg ttttatatgg agacacaggt gataaacaag caacccaagt gtcaattaaa 3060
aaagatttgg tttatgttct tgcagaggag aacaaaaata gtgtaaagca gcatataaaa 3120
atgactctag gtcaagattt aaaatcggac atctccttga atatagataa aataccagaa 3180
aaaaataatg attacatgaa caaatgggca ggactcttag gtccaatttc aaatcacagt 3240
tttggaggta gcttcagaac agcttcaaat aaggaaatca agctctctga acataacatt 3300
aagaagagca aaatgttctt caaagatatt gaagaacaat atcctactag tttagcttgt 3360
gttgaaattg taaatacctt ggcattagat aatcaaaaga aactgagcaa gcctcagtca 3420
attaatactg tatctgcaca tttacagagt agtgtagttg tttctgattg taaaaatagt 3480
catataaccc ctcagatgtt attttccaag caggatttta attcaaacca taatttaaca 3540
cctagccaaa aggcagaaat tacagaactt tctactatat tagaagaatc aggaagtcag 3600
tttgaattta ctcagtttag aaaaccaagc tacatattgc agaagagtac atttgaagtg 3660
cctgaaaacc agatgactat cttaaagacc acttctgagg aatgcagaga tgctgatctt 3720
catgtcataa tgaatgcccc atcgattggt caggtagaca gcagcaagca atttgaaggt 3780
acagttgaaa ttaaacggaa gtttgctggc ctgttgaaaa atgactgtaa caaaagtgct 3840
tctggttatt taacagatga aaatgaagtg gggtttaggg gcttttattc tgctcatggc 3900
acaaaactga atgtttctac tgaagctctg caaaaagctg tgaaactgtt tagtgatatt 3960
gagaatatta gtgaggaaac ttctgcagag gtacatccaa taagtttatc ttcaagtaaa 4020
tgtcatgatt ctgttgtttc aatgtttaag atagaaaatc ataatgataa aactgtaagt 4080
gaaaaaaata ataaatgcca actgatatta caaaataata ttgaaatgac tactggcact 4140
tttgttgaag aaattactga aaattacaag agaaatactg aaaatgaaga taacaaatat 4200
actgctgcca gtagaaattc tcataactta gaatttgatg gcagtgattc aagtaaaaat 4260
gatactgttt gtattcataa agatgaaacg gacttgctat ttactgatca gcacaacata 4320
tgtcttaaat tatctggcca gtttatgaag gagggaaaca ctcagattaa agaagatttg 4380
tcagatttaa ctttttggaa agttgcgaaa gctcaagaag catgtcatgg taatacttca 4440
aataaagaac agttaactgc tactaaaacg gagcaaaata taaaagattt tgagacttct 4500
gatacatttt ttcagactgc aagtgggaaa aatattagtg tcgccaaaga gtcatttaat 4560
aaaattgtaa atttctttga tcagaaacca gaagaattgc ataacttttc cttaaattct 4620
gaattacatt ctgacataag aaagaacaaa atggacattc taagttatga ggaaacagac 4680
atagttaaac acaaaatact gaaagaaagt gtcccagttg gtactggaaa tcaactagtg 4740
accttccagg gacaacccga acgtgatgaa aagatcaaag aacctactct gttgggtttt 4800
catacagcta gcgggaaaaa agttaaaatt gcaaaggaat ctttggacaa agtgaaaaac 4860
ctttttgatg aaaaagagca aggtactagt gaaatcacca gttttagcca tcaatgggca 4920
aagaccctaa agtacagaga ggcctgtaaa gaccttgaat tagcatgtga gaccattgag 4980
atcacagctg ccccaaagtg taaagaaatg cagaattctc tcaataatga taaaaacctt 5040
gtttctattg agactgtggt gccacctaag ctcttaagtg ataatttatg tagacaaact 5100
gaaaatctca aaacatcaaa aagtatcttt ttgaaagtta aagtacatga aaatgtagaa 5160
aaagaaacag caaaaagtcc tgcaacttgt tacacaaatc agtcccctta ttcagtcatt 5220
gaaaattcag ccttagcttt ttacacaagt tgtagtagaa aaacttctgt gagtcagact 5280
tcattacttg aagcaaaaaa atggcttaga gaaggaatat ttgatggtca accagaaaga 5340
ataaatactg cagattatgt aggaaattat ttgtatgaaa ataattcaaa cagtactata 5400
gctgaaaatg acaaaaatca tctctccgaa aaacaagata cttatttaag taacagtagc 5460
atgtctaaca gctattccta ccattctgat gaggtatata atgattcagg atatctctca 5520
aaaaataaac ttgattctgg tattgagcca gtattgaaga atgttgaaga tcaaaaaaac 5580
actagttttt ccaaagtaat atccaatgta aaagatgcaa atgcataccc acaaactgta 5640
aatgaagata tttgcgttga ggaacttgtg actagctctt caccctgcaa aaataaaaat 5700
gcagccatta aattgtccat atctaatagt aataattttg aggtagggcc acctgcattt 5760
aggatagcca gtggtaaaat cgtttgtgtt tcacatgaaa caattaaaaa agtgaaagac 5820
atatttacag acagtttcag taaagtaatt aaggaaaaca acgagaataa atcaaaaatt 5880
tgccaaacga aaattatggc aggttgttac gaggcattgg atgattcaga ggatattctt 5940
cataactctc tagataatga tgaatgtagc acgcattcac ataaggtttt tgctgacatt 6000
cagagtgaag aaattttaca acataaccaa aatatgtctg gattggagaa agtttctaaa 6060
atatcacctt gtgatgttag tttggaaact tcagatatat gtaaatgtag tatagggaag 6120
cttcataagt cagtctcatc tgcaaatact tgtgggattt ttagcacagc aagtggaaaa 6180
tctgtccagg tatcagatgc ttcattacaa aacgcaagac aagtgttttc tgaaatagaa 6240
gatagtacca agcaagtctt ttccaaagta ttgtttaaaa gtaacgaaca ttcagaccag 6300
ctcacaagag aagaaaatac tgctatacgt actccagaac atttaatatc ccaaaaaggc 6360
ttttcatata atgtggtaaa ttcatctgct ttctctggat ttagtacagc aagtggaaag 6420
caagtttcca ttttagaaag ttccttacac aaagttaagg gagtgttaga ggaatttgat 6480
ttaatcagaa ctgagcatag tcttcactat tcacctacgt ctagacaaaa tgtatcaaaa 6540
atacttcctc gtgttgataa gagaaaccca gagcactgtg taaactcaga aatggaaaaa 6600
acctgcagta aagaatttaa attatcaaat aacttaaatg ttgaaggtgg ttcttcagaa 6660
aataatcact ctattaaagt ttctccatat ctctctcaat ttcaacaaga caaacaacag 6720
ttggtattag gaaccaaagt ctcacttgtt gagaacattc atgttttggg aaaagaacag 6780
gcttcaccta aaaacgtaaa aatggaaatt ggtaaaactg aaactttttc tgatgttcct 6840
gtgaaaacaa atatagaagt ttgttctact tactccaaag attcagaaaa ctactttgaa 6900

39740-0001PCT.txt

acagaagcag tagaaattgc taaagctttt atggaagatg atgaactgac agattctaaa 6960
ctgccaagtc atgccacaca ttctcttttt acatgtcccg aaaatgagga aatggttttg 7020
tcaaattcaa gaattggaaa aagaagagga gagcccctta tcttagtggg agaaccctca 7080
atcaaaagaa acttattaaa tgaatttgac aggataatag aaaatcaaga aaaatcctta 7140
aaggcttcaa aaagcactcc agatggcaca ataaaagatc gaagattgtt tatgcatcat 7200
gtttctttag agccgattac ctgtgtaccc tttcgcacaa ctaaggaacg tcaagagata 7260
cagaatccaa attttaccgc acctggtcaa gaatttctgt ctaaatctca tttgtatgaa 7320
catctgactt tggaaaaatc ttcaagcaat ttagcagttt caggacatcc attttatcaa 7380
gtttctgcta caagaaatga aaaaatgaga cacttgatta ctacaggcag accaaccaaa 7440
gtctttgttc caccttttaa aactaaatca cattttcaca gagttgaaca gtgtgttagg 7500
aatattaact tggaggaaaa cagacaaaag caaaacattg atggacatgg ctctgatgat 7560
agtaaaaata agattaatga caatgagatt catcagttta acaaaaacaa ctccaatcaa 7620
gcagcagctg taactttcac aaagtgtgaa gaagaacctt tagatttaat tacaagtctt 7680
cagaatgcca gagatataca ggatatgcga attaagaaga aacaaaggca acgcgtcttt 7740
ccacagccag gcagtctgta tcttgcaaaa acatccactc tgcctcgaat ctctctgaaa 7800
gcagcagtag gaggccaagt tccctctgcg tgttctcata aacagctgta tacgtatggc 7860
gtttctaaac attgcataaa aattaacagc aaaaatgcag agtcttttca gtttcacact 7920
gaagattatt ttggtaagga aagtttatgg actggaaaag gaatacagtt ggctgatggt 7980
ggatggctca taccctccaa tgatggaaag gctggaaaag aagaatttta tagggctctg 8040
tgtgacactc caggtgtgga tccaaagctt atttctagaa tttgggttta taatcactat 8100
agatggatca tatggaaact ggcagctatg gaatgtgcct ttcctaagga atttgctaat 8160
agatgcctaa gcccagaaag ggtgcttctt caactaaaat acagatatga tacggaaatt 8220
gatagaagca gaagatcggc tataaaaaag ataatggaaa gggatgacac agctgcaaaa 8280
acacttgttc tctgtgtttc tgacataatt tcattgagcg caaatatatc tgaaacttct 8340
agcaataaaa ctagtagtgc agatacccaa aaagtggcca ttattgaact tacagatggg 8400
tggtatgctg ttaaggccca gttagatcct cccctcttag ctgtcttaaa gaatggcaga 8460
ctgacagttg gtcagaagat tattcttcat ggagcagaac tggtgggctc tcctgatgcc 8520
tgtacacctc ttgaagcccc agaatctctt atgttaaaga tttctgctaa cagtactcgg 8580
cctgctcgct ggtataccaa acttggattc tttcctgacc ctagaccttt tcctctgccc 8640
ttatcatcgc ttttcagtga tggaggaaat gttggttgtg ttgatgtaat tattcaaaga 8700
gcataccctа tacagtggat ggagaagaca tcatctggat tatacatatt tcgcaatgaa 8760
agagaggaag aaaaggaagc agcaaaatat gtggaggccc aacaaaagag actagaagcc 8820
ttattcacta aaattcagga ggaatttgaa gaacatgaag aaaacacaac aaaaccatat 8880
ttaccatcac gtgcactaac aagacagcaa gttcgtgctt tgcaagatgg tgcagagctt 8940
tatgaagcag tgaagaatgc agcagaccca gcttaccttg agggttattt cagtgaagag 9000
cagttaagag ccttgaataa tcacaggcaa atgttgaatg ataagaaaca agctcagatc 9060
cagttggaaa ttaggaaggc catggaatct gctgaacaaa aggaacaagg tttatcaagg 9120
gatgtcacaa ccgtgtggaa gttgcgtatt gtaagctatt caaaaaaaga aaaagattca 9180
gttatactga gtatttggcg tccatcatca gatttatatt ctctgttaac agaaggaaag 9240
agatacagaa tttatcatct tgcaacttca aaatctaaaa gtaaatctga aagagctaac 9300
atacagttag cagcgacaaa aaaaactcag tatcaacaac taccggtttc agatgaaatt 9360
ttatttcaga tttaccagcc acgggagccc cttcacttca gcaaattttt agatccagac 9420
tttcagccat cttgttctga ggtggaccta ataggatttg tcgtttctgt tgtgaaaaaa 9480
acaggacttg cccctttcgt ctatttgtca gacgaatgtt acaatttact ggcaataaag 9540
ttttggatag accttaatga ggacattatt aagcctcata tgttaattgc tgcaagcaac 9600
ctccagtggc gaccagaatc caaatcaggc cttcttactt tatttgctgg agatttttct 9660
gtgttttctg ctagtccaaa agagggccac tttcaagaga cattcaacaa aatgaaaaat 9720
actgttgaga atattgacat actttgcaat gaagcagaaa acaagcttat gcatatactg 9780
catgcaaatg atcccaagtg gtccacccca actaaagact gtacttcagg gccgtacact 9840
gctcaaatca ttcctggtac aggaaacaag cttctgatgt cttctcctaa ttgtgagata 9900
tattatcaaa gtcctttatc actttgtatg gccaaaagga agtctgtttc cacacctgtc 9960
tcagcccaga tgacttcaaa gtcttgtaaa ggggagaaag agattgatga ccaaaagaac 10020
tgcaaaaaga gaagagcctt ggatttcttg agtagactgc ctttacctcc acctgttagt 10080
cccatttgta catttgtttc tccggctgca cagaaggcat ttcagccacc aaggagttgt 10140
ggcaccaaat acgaaacacc cataaagaaa aaagaactga attctcctca gatgactcca 10200
tttaaaaaat tcaatgaaat ttctcttttg gaaagtaatt caatagctga cgaagaactt 10260
gcattgataa atacccaagc tcttttgtct ggttcaacag gagaaaaaca atttatatct 10320
gtcagtgaat ccactaggac tgctcccacc agttcagaag attatctcag actgaaacga 10380
cgttgtacta catctctgat caaagaacag gagagttccc aggccagtac ggaagaatgt 10440
gagaaaaata agcaggacac aattacaact aaaaaatata tctaagcatt tgcaaaggcg 10500
acaataaatt attgacgctt aacctttcca gtttataaga ctggaatata atttcaaacc 10560
acacattagt acttatgttg cacaatgaga aaagaaatta gtttcaaatt tacctcagcg 10620
tttgtgtatc gggcaaaaat cgttttgccc gattccgtat tggtatactt ttgcttcagt 10680
tgcatatctt aaaactaaat gtaatttatt aactaatcaa gaaaaacatc tttggctgag 10740
ctcggtggct catgcctgta atcccaacac tttgagaagc tgaggtggga ggagtgcttg 10800
aggccaggag ttcaagacca gcctgggcaa catagggaga cccccatctt tacgaagaaa 10860
aaaaaaaagg ggaaaagaaa atcttttaaa tctttggatt tgatcactac aagtattatt 10920
ttacaatcaa caaaatggtc atccaaactc aaacttgaga aaatatcttg ctttcaaatt 10980

gacacta 10987

<210> 291
<211> 1552
<212> DNA
<213> Homo sapiens

<400> 291
gcccgtacac accgtgtgct gggacacccc acagtcagcc gcatggctcc cctgtgcccc 60
agcccctggc tccctctgtt gatcccggcc cctgctccag gcctcactgt gcaactgctg 120
ctgtcactgc tgcttctgat gcctgtccat ccccagaggt tgccccggat gcaggaggat 180
tccccccttgg gaggaggctc ttctggggaa gatgacccac tgggcgagga ggatctgccc 240
agtgaagagg attcacccag agaggaggat ccacccggag aggaggatct acctggagag 300
gaggatctac ctggagagga ggatctacct gaagttaagc ctaaatcaga agaagagggc 360
tccctgaagt tagaggatct acctactgtt gaggctcctg gagatcctca agaaccccag 420
aataatgccc acagggacaa agaaggggat gaccagagtc attggcgcta tggaggcgac 480
ccgccctggc cccgggtgtc cccagcctgc gcgggccgct tccagtcccc ggtggatatc 540
cgccccccagc tcgccgcctt ctgcccggcc ctgcgccccc tggaactcct gggcttccag 600
ctcccgccgc tcccagaact gcgcctgcgc aacaatggcc acagtgtgca actgaccctg 660
cctcctgggc tagagatggc tctgggtccc gggcgggagt accgggctct gcagctgcat 720
ctgcactggg gggctgcagg tcgtccgggc tcggagcaca ctgtggaagg ccaccgtttc 780
cctgccgaga tccacgtggt tcacctcagc accgcctttg ccagagttga cgaggccttg 840
gggcgcccgg gaggcctggc cgtgttggcc gcctttctgg aggagggccc ggaagaaaac 900
agtgcctatg agcagttgct gtctcgcttg gaagaaatcg ctgaggaagg ctcagagact 960
caggtcccag gactggacat atctgcactc ctgccctctg acttcagccg ctacttccaa 1020
tatgaggggt ctctgactac accgccctgt gcccagggtg tcatctggac tgtgtttaac 1080
cagacagtga tgctgagtgc taagcagctc cacaccctct ctgacaccct gtggggacct 1140
ggtgactctc ggctacagct gaacttccga gcgacgcagc ctttgaatgg gcgagtgatt 1200
gaggcctcct tccctgctgg agtggacagc agtcctcggg ctgctgagcc agtccagctg 1260
aattcctgcc tggctgctgg tgacatccta gccctggttt ttggcctcct ttttgctgtc 1320
accagcgtcg cgttccttgt gcagatgaga aggcagcaca gaaggggaac caaagggggt 1380
gtgagctacc gcccagcaga ggtagccgag actggagcct agaggctgga tcttggagaa 1440
tgtgagaagc cagccagagg catctgaggg ggagccggta actgtcctgt cctgctcatt 1500
atgccacttc cttttaactg ccaagaaatt ttttaaaata aatatttata at 1552

<210> 292
<211> 1578
<212> DNA
<213> Homo sapiens

<400> 292
acgaacaggc caataaggag ggagcagtgc ggggtttaaa tctgaggcta ggctggctct 60
tctcggcgtg ctgcggcgga acggctgttg gtttctgctg gttgtaggtc cttggctggt 120
cgggcctccg gtgttctgct tctccccgct gagctgctgc ctggtgaaga ggaagccatg 180
gcgctccgag tcaccaggaa ctcgaaaatt aatgctgaaa ataaggcgaa gatcaacatg 240
gcaggcgcaa agcgcgttcc tacggcccct gctgcaacct ccaagcccgg actgaggcca 300
agaacagctc ttggggacat tggtaacaaa gtcagtgaac aactgcaggc caaaatgcct 360
atgaagaagg aagcaaaacc ttcagctact ggaaaagtca ttgataaaaa actaccaaaa 420
cctcttgaaa aggtacctat gctggtgcca gtgccagtgt ctgagccagt gccagagcca 480
gaacctgagc cagaacctga gcctgttaaa gaagaaaaac tttcgcctga gcctattttg 540
gttgatactg cctctccaag cccaatggaa acatctggat gtgcccctgc agaagaagac 600
ctgtgtcagg ctttctctga tgtaattctt gcagtaaatg atgtggatgc agaagatgga 660
gctgatccaa acctttgtag tgaatatgtg aaagatattt atgcttatct gagacaactt 720
gaggaagagc aagcagtcag accaaaatac ctactgggtc gggaagtcac tggaaacatg 780
agagccatcc taattgactg gctagtacag gttcaaatga aattcaggtt gttgcaggag 840
accatgtaca tgactgtctc cattattgat cggttcatgc agaataattg tgtgcccaag 900
aagatgctgc agctggttgg tgtcactgcc atgtttattg caagcaaata tgaagaaatg 960
taccctccag aaattggtga ctttgctttt gtgactgaca acacttatac taagcaccaa 1020
atcagacaga tggaaatgaa gattctaaga gctttaaact ttggtctggg tcggcctcta 1080
cctttgcact tccttcggag agcatctaag attggagagg ttgatgtcga gcaacatact 1140
ttggccaaat acctgatgga actaactatg ttggactatg acatggtgca ctttcctcct 1200
tctcaaattg cagcaggagc tttttgctta gcactgaaaa ttctggataa tggtgaatgg 1260
acaccaactc tacaacatta cctgtcatat actgaagaat ctcttcttcc agttatgcag 1320
cacctggcta agaatgtagt catggtaaat caaggactta caaagcacat gactgtcaag 1380
aacaagtatg ccacatcgaa gcatgctaag atcagcactc taccacagct gaattctgca 1440
ctagttcaag atttagccaa ggctgtggca aaggtgtaac ttgtaaactt gagttggagt 1500

actatattta caaataaaat tggcaccatg tgccatctgt aaaaaaaaaa aaaaaaaaaa 1560
aaaaaaaaaa aaaaaaaa 1578

<210> 293
<211> 3195
<212> DNA
<213> Homo sapiens

<400> 293
agaggcttcc ctggctggtg cctgagcccg gcgtccctcg cccccccgccc tccccgcatc 60
cctctcctcc ctcgcgcctg gccctgtggc tcttcctccc tccctccttc cccccccccc 120
caccccctcgc ccgctgcctc cctcggccca gccagctgtg ccggcgtttg ttggctgccc 180
tgcgcccggc cctccagcca gccttctgcc ggccccgccg cgatggaggt gccccagccg 240
gagcccgcgc caggctcggc tctcagtcca gcaggcgtgt gcggtggcgc ccagcgtccg 300
ggccacctcc cgggcctcct gctgggatct catggcctcc tggggtcccc ggtgcgggcg 360
gccgcttcct cgccggtcac caccctcacc cagaccatgc acgacctcgc cgggctcggc 420
agccgcagcc gcctgacgca cctatccctg tctcgacggg catccgaatc ctccctgtcg 480
tctgaatcct ccgaatcttc tgatgcaggt ctctgcatgg attcccccag ccctatggac 540
ccccacatgg cggagcagac gtttgaacag gccatccagg cagccagccg gatcattcga 600
aacgagcagt ttgccatcag acgcttccag tctatgccgg tgaggctgct gggccacagc 660
cccgtgcttc ggaacatcac caactcccag gcgcccgacg gccggaggaa gagcgaggcg 720
ggcagtggag ctgccagcag ctctggggaa gacaaggaga atgtgcgctt ctggaaggcc 780
ggggtgggag ctctccggga agaggagggg gcatgctggg gtggttccct ggcatgtgag 840
gaccctcctc tcccatcttg gctgcaggat ggatttgtct tcaagatgcc atggaagccc 900
acacatccca gctccaccca tgctctggca gagtggccca gccgcaggga agcctttgcc 960
cagagaccca gctcggcccc cgacctgatg tgtctcagtc ctgaccggaa gatggaagtg 1020
gaggagctca gccccctggc cctaggtcgc ttctctctga cccctgcaga gggggatact 1080
gaggaagatg atggatttgt ggacatccta gagagtgact taaaggatga tgatgcagtt 1140
cccccaggca tggagagtct cattagtgcc ccactggtca agaccttgga aaaggaagag 1200
gaaaaggacc tcgtcatgta cagcaagtgc cagcggctct tccgctctcc gtccatgccc 1260
tgcagcgtga tccggcccat cctcaagagg ctggagcggc cccaggacag ggacacgccc 1320
gtgcagaata agcggaggcg gagcgtgacc cctcctgagg agcagcagga ggctgaggaa 1380
cctaaagccc gcgtcctccg ctcaaaatca ctgtgtcacg atgagatcga gaacctcctg 1440
gacagtgacc accgagagct gattggagat tactctaagg ccttcctcct acagacagta 1500
gacggaaagc accaagacct caagtacatc tcaccagaaa cgatggtggc cctattgacg 1560
ggcaagttca gcaacatcgt ggataagttt gtgattgtag actgcagata cccctatgaa 1620
tatgaaggcg ggcacatcaa gactgcggtg aacttgcccc tggaacgcga cgccgagagc 1680
ttcctactga agagccccat cgcgccctgt agcctggaca agagagtcat cctcatttc 1740
cactgtgaat tctcatctga gcgtgggccc cgcatgtgcc gtttcatcag ggaacgagac 1800
cgtgctgtca acgactaccc cagcctctac taccctgaga tgtatatcct gaaaggcggc 1860
tacaaggagt tcttccctca gcacccgaac ttctgtgaac cccaggacta ccggcccatg 1920
aaccacgagg ccttcaagga tgagctaaag accttccgcc tcaagactcg cagctgggct 1980
ggggagcgga gccggcggga gctctgtagc cggctgcagg accagtgagg ggcctgcgcc 2040
agtcctgcta cctcccttgc ctttcgaggc ctgaagccag ctgccctatg ggcctgccgg 2100
gctgagggcc tgctggaggc ctcaggtgct gtccatggga aagatggtgt ggtgtcctgc 2160
ctgtctgccc cagcccagat tcccctgtgt catcccatca ttttccatat cctggtgccc 2220
cccacccctg gaagagccca gtctgttgag ttagttaagt tgggttaata ccagcttaaa 2280
ggcagtattt tgtgtcctcc aggagcttct tgtttccttg ttagggttaa cccttcatct 2340
tcctgtgtcc tgaaacgctc ctttgtgtgt gtgtcagctg aggctgggga gagccgtggt 2400
ccctgaggat gggtcagagc taaactcctt cctggcctga gagtcagctc tctgccctgt 2460
gtacttcccg ggccagggct gccccctaatc tctgtaggaa ccgtggtatg tctgccatgt 2520
tgcccctttc tcttttcccc tttcctgtcc caccatacga gcacctccag cctgaacaga 2580
agctcttact ctttcctatt tcagtgttac ctgtgtgctt ggtctgtttg actttacgcc 2640
catctcagga cacttccgta gactgtttag gttcccctgt caaatatcag ttacccactc 2700
ggtcccagtt ttgttgcccc agaaagggat gttattatcc ttgggggctc ccagggcaag 2760
ggttaaggcc tgaatcatga gcctgctgga agcccagccc ctactgctgt gaaccctggg 2820
gcctgactgc tcagaacttg ctgctgtctt gttgcggatg gatggaaggt tggatggatg 2880
ggtggatggc cgtggatggc cgtggatgcg cagtgccttg catacccaaa ccaggtggga 2940
gcgttttgtt gagcatgaca cctgcagcag gaatatatgt gtgcctattt gtgtggacaa 3000
aaatatttac acttagggtt tggagctatt caagaggaaa tgtcacagaa gcagctaaac 3060
caaggactga gcaccctctg gattctgaat ctcaagatgg gggcagggct gtgcttgaag 3120
gccctgctga gtcatctgtt agggccttgg ttcaataaag cactgagcaa gttgagaaaa 3180
aaaaaaaaaa aaaaa 3195

<210> 294
<211> 3737
<212> DNA
<213> Homo sapiens

<400> 294
ggcgtccgcg cacacctccc cgcgccgccg ccgccaccgc ccgcactccg ccgcctctgc 60
ccgcaaccgc tgagccatcc atgggggtcg cgggccgcaa ccgtcccggg gcggcctggg 120
cggtgctgct gctgctgctg ctgctgccgc cactgctgct gctggcgggg gccgtcccgc 180
cgggtcgggg ccgtgccgcg gggccgcagg aggatgtaga tgagtgtgcc caagggctag 240
atgactgcca tgccgacgcc ctgtgtcaga acacacccac ctcctacaag tgctcctgca 300
agcctggcta ccaaggggaa ggcaggcagt gtgaggacat cgatgaatgt ggaaatgagc 360
tcaatggagg ctgtgtccat gactgtttga atattccagg caattatcgt tgcacttgtt 420
ttgatggctt catgttggct catgacggtc ataattgtct tgatgtggac gagtgcctgg 480
agaacaatgg cggctgccag catacctgtg tcaacgtcat ggggagctat gagtgctgct 540
gcaaggaggg gtttttcctg agtgacaatc agcacacctg cattcaccgc tcggaagagg 600
gcctgagctg catgaataag gatcacggct gtagtcacat ctgcaaggag gccccaaggg 660
gcagcgtcgc ctgtgagtgc aggcctggtt ttgagctggc caagaaccag agagactgca 720
tcttgacctg taaccatggg aacggtgggt gccagcactc ctgtgacgat acagccgatg 780
gcccagagtg cagctgccat ccacagtaca agatgcacac agatgggagg agctgccttg 840
agcgagagga cactgtcctg gaggtgacag agagcaacac cacatcagtg gtggatgggg 900
ataaacgggt gaaacggcgg ctgctcatgg aaacgtgtgc tgtcaacaat ggaggctgtg 960
accgcacctg taaggatact tcgacaggtg tccactgcag ttgtcctgtt ggattcactc 1020
tccagttgga tgggaagaca tgtaaagata ttgatgagtg ccagacccgc aatggaggtt 1080
gtgatcattt ctgcaaaaac atcgtgggca gttttgactg cggctgcaag aaaggattta 1140
aattattaac agatgagaag tcttgccaag atgtggatga gtgctctttg gataggacct 1200
gtgaccacag ctgcatcaac caccctggca catttgcttg tgcttgcaac cgagggtaca 1260
ccctgtatgg cttcacccac tgtggagaca ccaatgagtg cagcatcaac aacggaggct 1320
gtcagcaggt ctgtgtgaac acagtgggca gctatgaatg ccagtgccac cctgggtaca 1380
agctccactg gaataaaaaa gactgtgtgg aagtgaaggg gctcctgccc acaagtgtgt 1440
caccccgtgt gtccctgcac tgcggtaaga gtggtggagg agacgggtgc ttcctcagat 1500
gtcactctgg cattcacctc tcttcagatg tcaccaccat caggacaagt gtaaccttta 1560
agctaaatga aggcaagtgt agtttgaaaa atgctgagct gtttcccgag ggtctgcgac 1620
cagcactacc agagaagcac agctcagtaa aagagagctt ccgctacgta aaccttacat 1680
gcagctctgg caagcaagtc ccaggagccc ctggccgacc aagcacccct aaggaaatgt 1740
ttatcactgt tgagtttgag cttgaaacta accaaaagga ggtgacagct tcttgtgacc 1800
tgagctgcat cgtaaagcga accgagaagc ggctccgtaa agccatccgc acgctcagaa 1860
aggccgtcca cagggagcag tttcacctcc agctctcagg catgaacctc gacgtggcta 1920
aaaagcctcc cagaacatct gaacgccagg cagagtcctg tggagtgggc cagggtcatg 1980
cagaaaacca atgtgtcagt tgcagggctg ggacctatta tgatggagca cgagaacgct 2040
gcattttatg tccaaatgga accttccaaa atgaggaagg acaaatgact tgtgaaccat 2100
gcccaagacc aggaaattct ggggccctga agaccccaga agcttggaat atgtctgaat 2160
gtggaggtct gtgtcaacct ggtgaatatt ctgcagatgg ctttgcacct tgccagctct 2220
gtgccctggg cacgttccag cctgaagctg gtcgaacttc ctgcttcccc tgtggaggag 2280
gccttgccac caaacatcag ggagctactt cctttcagga ctgtgaaacc agagttcaat 2340
gttcacctgg acatttctac aacaccacca ctcaccgatg tattcgttgc ccagtgggaa 2400
cataccagcc tgaatttgga aaaaataatt gtgtttcttg cccaggaaat actacgactg 2460
actttgatgg ctccacaaac ataacccagt gtaaaaacag aagatgtgga ggggagctgg 2520
gagatttcac tgggtacatt gaatccccaa actacccagg caattaccca gccaacaccg 2580
agtgtacgtg gaccatcaac ccacccccca agcgccgcat cctgatcgtg gtccctgaga 2640
tcttcctgcc catagaggac gactgtgggg actatctggt gatgcggaaa acctcttcat 2700
ccaattctgt gacaacatat gaaacctgcc agacctacga acgccccatc gccttcacct 2760
ccaggtcaaa gaagctgtgg attcagttca agtccaatga agggaacagc gctagagggt 2820
tccaggtccc atacgtgaca tatgatgagg actaccagga actcattgaa gacatagttc 2880
gagatggcag gctctatgca tctgagaacc atcaggaaat acttaaggat aagaaactta 2940
tcaaggctct gtttgatgtc ctggcccatc cccagaacta tttcaagtac acagcccagg 3000
agtcccgaga gatgtttcca agatcgttca tccgattgct acgttccaaa gtgtccaggt 3060
ttttgagacc ttacaaatga ctcagcccac gtgccactca atacaaatgt tctgctatag 3120
ggttggtggg acagagctgt cttccttctg catgtcagca cagtcgggta ttgctgcctc 3180
ccgtatcagt gactcattag agttcaattt ttatagataa tacagatatt ttggtaaatt 3240
gaacttggtt tttctttccc agcatcgtgg atgtagactg agaatggctt tgagtggcat 3300
cagcttctca ctgctgtggg cggatgtctt ggatagatca cgggctggct gagctggact 3360
ttggtcagcc taggtgagac tcacctgtcc ttctggggtc ttactcctcc tcaaggagtc 3420
tgtagtggaa aggaggccac agaataagct gcttattctg aaacttcagc ttcctctagc 3480
ccggccctct ctaagggagc cctctgcact cgtgtgcagg ctctgaccag gcagaacagg 3540
caagagggga gggaaggaga cccctgcagg ctccctccac ccaccttgag acctgggagg 3600
actcagtttc tccacagcct tctccagcct gtgtgataca agtttgatcc caggaacttg 3660
agttctaagc agtgctcgtg aaaaaaaaaa gcagaaagaa ttagaaataa ataaaaacta 3720
agcacttctg gagacat 3737

<210> 295
<211> 2042

<212> DNA
<213> Homo sapiens

<400> 295
ggggccagtc gttcgccgga aagcatttgt ctcccacctc atcataacaa caattaattt 60
cctctggggc ctgaggaggg cagaatttca accttcggtg tgcttgggag tggcgattgt 120
gatttacacg acaaaatgcc gaggtgctcg gtggagtcat ggcagtgccc tttgtggaag 180
actgggactt ggtgcaaacc ctgggagaag gtgcctatgg agaagttcaa cttgctgtga 240
atagagtaac tgaagaagca gtcgcagtga agattgtaga tatgaagcgt gccgtagact 300
gtccagaaaa tattaagaaa gagatctgta tcaataaaat gctaaatcat gaaaatgtag 360
taaaattcta tggtcacagg agagaaggca atatccaata tttatttctg gagtactgta 420
gtggaggaga gctttttgac agaatagagc cagacatagg catgcctgaa ccagatgctc 480
agagattctt ccatcaactc atggcagggg tggtttatct gcatggtatt ggaataactc 540
acagggatat taaaccagaa aatcttctgt tggatgaaag ggataacctc aaaatctcag 600
actttggctt ggcaacagta tttcggtata ataatcgtga gcgtttgttg aacaagatgt 660
gtggtacttt accatatgtt gctccagaac ttctgaagag aagagaattt catgcagaac 720
cagttgatgt ttggtcctgt ggaatagtac ttactgcaat gctcgctgga gaattgccat 780
gggaccaacc cagtgacagc tgtcaggagt attctgactg gaaagaaaaa aaaacatacc 840
tcaacccttg gaaaaaaatc gattctgctc ctctagctct gctgcataaa atcttagttg 900
agaatccatc agcaagaatt accattccag acatcaaaaa agatagatgg tacaacaaac 960
ccctcaagaa aggggcaaaa aggccccgag tcacttcagg tggtgtgtca gagtctccca 1020
gtggattttc taagcacatt caatccaatt tggacttctc tccagtaaac agtgcttcta 1080
gtgaagaaaa tgtgaagtac tccagttctc agccagaacc ccgcacaggt ctttccttat 1140
gggataccag cccctcatac attgataaat tggtacaagg gatcagcttt tcccagccca 1200
catgtcctga tcatatgctt ttgaatagtc agttacttgg caccccagga tcctcacaga 1260
acccctggca gcggttggtc aaaagaatga cacgattctt taccaaattg gatgcagaca 1320
aatcttatca atgcctgaaa gagacttgtg agaagttggg ctatcaatgg aagaaaagtt 1380
gtatgaatca ggttactata tcaacaactg ataggagaaa caataaactc attttcaaag 1440
tgaatttgtt agaaatggat gataaaatat tggttgactt ccggctttct aagggtgatg 1500
gattggagtt caagagacac ttcctgaaga ttaaagggaa gctgattgat attgtgagca 1560
gccagaaggt ttggcttcct gccacatgat cggaccatcg gctctgggga atcctggtga 1620
atatagtgct gctatgttga cattattctt cctagagaag attatcctgt cctgcaaact 1680
gcaaatagta gttcctgaag tgttcacttc cctgtttatc caaacatctt ccaatttatt 1740
ttgtttgttc ggcatacaaa taatacctat atcttaattg taagcaaaac tttggggaaa 1800
ggatgaatag aattcatttg attatttctt catgtgtgtt tagtatctga atttgaaact 1860
catctggtgg aaaccaagtt tcaggggaca tgagttttcc agcttttata cacacgtatc 1920
tcatttttat caaaacattt tgtttaattc aaaaagtaca tatttcttcc atgttgattt 1980
aattctaaga tgaaccaata aagacataat tcttgcaaaa aaaaaaaaaa aaaaaaaaaa 2040
aa 2042

<210> 296
<211> 2547
<212> DNA
<213> Homo sapiens

<400> 296
cttacaaggt acagtcctct gctcaggggg gccaggaggg tcttataggc atcattcacc 60
agggtcgaat gcttctctga gaagtccttt tcagtctgag acctctggct gaagaaatct 120
gggtggacaa gacgctgcag ttgctggtac ctgtgctgga gcttcgctgt atcaactctg 180
aaggaacggt tgcagtccat aaggctgaag tagtctcgag tggggtcagg tgcctgcagc 240
gctcggcact gtgggcagaa gaacctgtcc tcccgcccgg ggccccatgg gccgccgcag 300
ttccaacagc ggggataatt gcttcccgcc tgcgacgcag catcgcagct tagcggtctc 360
cttctgggaa cccctgtcgg ccaaaacccc cacacccgga gcaaagcccc ggctctcccc 420
cgccacatct ggccggcggc ctatctagcc gtggtcactc gtggggaaaa gcaaagagag 480
cgtctaacca gactaatgtt gctgattggc tggggagtcg agggggcggg atcacccgag 540
gggaacccgg gttctaagtt ccgctctccc ttctaaacta caactcccag gaggcattga 600
ggcggcgcct gacggccaca tctgctgctc ctcattggtc cggcggcagg ggagggggtt 660
ttgattggct gagggtggag tttgtatctg caggtttagc gccactctgc tggctgaggc 720
tgcggagagt gtgcggctcc aggtgggctc acgcggtcgt gatgtctcgg gagtcggatg 780
ttgaggctca gcagtctcat ggcagcagtg cctgttcaca gccccatggc agcgttaccc 840
agtcccaagg ctcctcctca cagtcccagg gcatatccag ctcctctacc agcacgatgc 900
caaactccag ccagtcctct cactccagct ctgggacact gagctcctta gagacagtgt 960
ccactcagga actctattct attcctgagg accaagaacc tgaggaccaa gaacctgagg 1020
agcctacccc tgccccctgg gctcgattat gggcccttca ggatggattt gccaatcttg 1080
aatgtgtgaa tgacaactac tggtttggga gggacaaaag ctgtgaatat tgctttgatg 1140
aaccactgct gaaaagaaca gataaatacc gaacatacag caagaaacac tttcggattt 1200
tcagggaagt gggtcctaaa aactcttaca ttgcatacat agaagatcac agtggcaatg 1260
gaacctttgt aaatacagag cttgtaggga aaggaaaacg ccgtcctttg aataacaatt 1320

ctgaaattgc actgtcacta agcagaaata aagtttttgt ctttttgat ctgactgtag 1380
atgatcagtc agtttatcct aaggcattaa gagatgaata catcatgtca aaaactcttg 1440
gaagtggtgc ctgtggagag gtaaagctgg ctttcgagag gaaaacatgt aagaaagtag 1500
ccataaagat catcagcaaa aggaagtttg ctattggttc agcaagagag gcagacccag 1560
ctctcaatgt tgaaacagaa atagaaattt tgaaaaagct aaatcatcct tgcatcatca 1620
agattaaaaa ctttttgat gcagaagatt attatattgt tttggaattg atggaagggg 1680
gagagctgtt tgacaaagtg gtggggaata aacgcctgaa agaagctacc tgcaagctct 1740
atttttacca gatgctcttg gctgtgcagt accttcatga aaacggtatt atacaccgtg 1800
acttaaagcc agagaatgtt ttactgtcat ctcaagaaga ggactgtctt ataaagatta 1860
ctgatttgg gcactccaag attttgggag agacctctct catgagaacc ttatgtggaa 1920
cccccaccta cttggcgcct gaagttcttg tttctgttgg gactgctggg tataaccgtg 1980
ctgtggactg ctggagttta ggagttattc tttttatctg ccttagtggg tatccacctt 2040
tctctgagca taggactcaa gtgtcactga aggatcagat caccagtgga aaatacaact 2100
tcattcctga agtctgggca gaagtctcag agaaagctct ggaccttgtc aagaagttgt 2160
tggtagtgga tccaaaggca cgttttacga cagaagaagc cttaagacac ccgtggcttc 2220
aggatgaaga catgaagaga aagtttcaag atcttctgtc tgaggaaaat gaatccacag 2280
ctctacccca ggttctagcc cagccttcta ctagtcgaaa gcggccccgt gaaggggaag 2340
ccgagggtgc cgagaccaca aagcgcccag ctgtgtgtgc tgctgtgttg tgaactccgt 2400
ggtttgaaca cgaaagaaat gtaccttctt tcactctgtc atctttcttt tctttgagtc 2460
tgttttttta tagtttgtat tttaattatg ggaataattg ctttttcaca gtcactgatg 2520
tacaattaaa aacctgatgg aacctgg 2547

<210> 297
<211> 2768
<212> DNA
<213> Homo sapiens

<400> 297
cactgctgtg cagggcagga aagctccatg cacatagccc agcaaagagc aacacagagc 60
tgaaaggaag actcagagga gagagataag taaggaaagt agtgatggct ctcatcccag 120
acttggccat ggaaacctgg cttctcctgg ctgtcagcct ggtgctcctc tatctatatg 180
gaacccattc acatggactt tttaagaagc ttggaattcc agggcccaca cctctgcctt 240
ttttgggaaa tattttgtcc taccataagg gcttttgtat gtttgacatg gaatgtcata 300
aaaagtatgg aaaagtgtgg ggcttttatg atggtcaaca gcctgtgctg gctatcacag 360
atcctgacat gatcaaaaca gtgctagtga aagaatgtta ttctgtcttc acaaaccgga 420
ggcctttgg tccagtggga tttatgaaaa gtgccatctc tatagctgag gatgaagaat 480
ggaagagatt acgatcattg ctgtctccaa ccttcaccag tggaaaactc aaggagatgg 540
tccctatcat tgcccagtat ggagatgtgt tggtgagaaa tctgaggcgg gaagcagaga 600
caggcaagcc tgtcaccttg aaagacgtct ttggggccta cagcatggat gtgatcacta 660
gcacatcatt tggagtgaac atcgactctc tcaacaatcc acaagacccc tttgtggaaa 720
acaccaagaa gcttttaaga tttgattttt tggatccatt ctttctctca ataacagtct 780
ttccattcct catcccaatt cttgaagtat taaatatctg tgtgtttcca agagaagtta 840
caaatttttt aagaaaatct gtaaaaagga tgaaagaaag tcgcctcgaa gatacacaaa 900
agcaccgagt ggatttcctt cagctgatga ttgactctca gaattcaaaa gaaactgagt 960
cccacaaagc tctgtccgat ctggagctcg tggcccaatc aattatcttt atttttgctg 1020
gctatgaaac cacgagcagt gttctctcct tcattatgta tgaactggcc actcaccctg 1080
atgtccagca gaaactgcag gaggaaattg atgcagtttt acccaataag gcaccaccca 1140
cctatgatac tgtgctacag atggagtatc ttgacatggt ggtgaatgaa acgctcagat 1200
tattcccaat tgctatgaga cttgagaggg tctgcaaaaa agatgttgag atcaatggga 1260
tgttcattcc caaaggggtg gtggtgatga ttccaagcta tgctcttcac cgtgacccaa 1320
agtactggac agagcctgag aagttcctcc ctgaaagatt cagcaagaag aacaaggaca 1380
acatagatcc ttacatatac acaccctttg gaagtggacc cagaaactgc attggcatga 1440
ggtttgctct catgaacatg aaacttgctc taatcagagt ccttcagaac ttctccttca 1500
aaccttgtaa agaaacacag atcccctga aattaagctt aggaggactt cttcaaccag 1560
aaaaacccgt tgttctaaag gttgagtcaa gggatggcac cgtaagtgga gcctgaattt 1620
tcctaaggac ttctgctttg ctcttcaaga aatctgtgcc tgagaacacc agagacctca 1680
aattactttg tgaatagaac tctgaaatga agatgggctt catccaatgg actgcataaa 1740
taaccgggga ttctgtacat gcattgagct ctctcattgt ctgtgtagag tgttatactt 1800
gggaatataa aggaggtgac caaatcagtg tgaggaggta gatttggctc ctctgcttct 1860
cacgggacta tttccaccac ccccagttag caccattaac tcctcctgag ctctgataag 1920
agaatcaaca tttctcaata atttcctcca caaattatta atgaaaataa gaattatttt 1980
gatggctcta acaatgacat ttatatcaca tgttttctct ggagtattct ataagtttta 2040
tgttaaatca ataaagacca ctttacaaaa gtattatcag atgctttcct gcacattaag 2100
gagaaatcta tagaactgaa tgagaaccaa caagtaaata tttttggtca ttgtaatcac 2160
tgttggcgtg gggcctttgt cagaactaga atttgattat taacataggt gaaagttaat 2220
ccactgtgac tttgcccatt gtttagaaag aatattcata gtttaattat gcctttttg 2280
atcaggcaca gtggctcacg cctgtaatcc tagcagtttg ggaggctgag ccgggtggat 2340
cgcctgaggt caggagttca agacaagcct ggcctacatg gttgaaaccc catctctact 2400

aaaaatacac aaattagcta ggcatggtgg actcgcctgt aatctcacta cacaggaggc 2460
tgaggcagga gaatcacttg aacctgggag gcggatgttg aagtgagctg agattgcacc 2520
actgcactcc agtctgggtg agagtgagac tcagtcttaa aaaaatatgc cttttgaag 2580
cacgtacatt ttgtaacaaa gaactgaagc tcttattata ttattagttt tgatttaatg 2640
ttttcagccc atctcctttc atatttctgg gagacagaaa acatgtttcc ctacacctct 2700
tgcattccat cctcaacacc caactgtctc gatgcaatga acacttaata aaaaacagtc 2760
gattggtc 2768

<210> 298
<211> 1358
<212> DNA
<213> Homo sapiens

<400> 298
ggcgtccgcg cgctgcacaa tggcggctct gaagagttgg ctgtcgcgca gcgtaacttc 60
attcttcagg tacagacagt gtttgtgtgt tcctgttgtg gctaacttta agaagcggtg 120
tttctcagaa ttgataagac catggcacaa aactgtgacg attggctttg gagtaaccct 180
gtgtgcggtt cctattgcac agaaatcaga gcctcattcc cttagtagtg aagcattgat 240
gaggagagca gtgtctttgg taacagatag cacctctacc tttctctctc agaccacata 300
tgcgttgatt gaagctatta ctgaatatac taaggctgtt tataccttaa cttctcttta 360
ccgacaatat acaagtttac ttgggaaaat gaattcagag gaggaagatg aagtgtggca 420
ggtgatcata ggagccagag ctgagatgac ttcaaaacac caagagtact tgaagctgga 480
aaccacttgg atgactgcag ttggtctttc agagatggca gcagaagctg catatcaaac 540
tggcgcagat caggcctcta taaccgccag gaatcacatt cagctggtga aactgcaggt 600
ggaagaggtg caccagctct cccggaaagc agaaaccaag ctggcagaag cacagataga 660
agagctccgt cagaaaacac aggaggaagg ggaggagcgg gctgagtcgg agcaggaggc 720
ctacctgcgt gaggattgag ggcctgagca cactgccctg tctccccact cagtggggaa 780
agcaggggca gatgccaccc tgcccagggt tggcatgact gtctgtgcac cgagaagagg 840
cggcaggtcc tgccctggcc aatcaggcga gacgcctttg tgagctgtga gtgcctcctg 900
tggtctcagg cttgcgctgg acctggttct tagcccttgg gcactgcacc ctgtttaaca 960
tttcacccca ctctgtacag ctgctcttac ccattttttt tacctcacac ccaaagcatt 1020
ttgcctacct gggtcagaga gaggagtcct ttttgtcatg cccttaagtt cagcaactgt 1080
ttaacctgtt ttcagtctta tttacgtcgt caaaaatgat ttagtacttg ttccctctgt 1140
tgggatgcca gttgtggcag ggggaggggа acctgtccag tttgtacgat ttctttgtat 1200
gtatttctga tgtgttctct gatctgcccc cactgtcctg tgaggacagc tgaggccaag 1260
gagtgaaaaa cctattacta ctaagagaag gggtgcagag tgtttacctg gtgctctcaa 1320
caggacttaa catcaacagg acttaacaca gaaaaaaa 1358

<210> 299
<211> 4407
<212> DNA
<213> Homo sapiens

<400> 299
tttcgactcg cgctccggct gctgtcactt ggctctctgg ctggagcttg aggacgcaag 60
gagggtttgt cactggcaga ctcgagactg taggcactgc catggcccct gtgctcagta 120
aggactcggc ggacatcgag agtatcctgg ctttaaatcc tcgaacacaa actcatgcaa 180
ctctgtgttc cacttcggcc aagaaattag acaagaaaca ttggaaaaga aatcctgata 240
agaactgctt taattgtgag aagctggaga ataattttga tgacatcaag cacacgactc 300
ttggtgagcg aggagctctc cgagaagcaa tgagatgcct gaaatgtgca gatgccccgt 360
gtcagaagag ctgtccaact aatcttgata ttaaatcatt catcacaagt attgcaaaca 420
agaactatta tggagctgct aagatgatat tttctgacaa cccacttggt ctgacttgtg 480
gaatggtatg tccaacctct gatctatgtg taggtggatg caatttatat gccactgaag 540
agggacccat taatattggt ggattgcagc aatttgctac tgaggtattc aaagcaatga 600
gtatcccaca gatcagaaat ccttcgctgc ctcccccaga aaaaatgtct gaagcctatt 660
ctgcaaagat tgctcttttt ggtgctgggc ctgcaagtat aagttgtgct tccttttttgg 720
ctcgattggg gtactctgac atcactatat ttgaaaaaca agaatatgtt ggtggtttaa 780
gtacttctga aattcctcag ttccggctgc cgtatgatgt agtgaatttt gagattgagc 840
taatgaagga ccttggtgta aagataattt gcggtaaaag cctttcagtg aatgaaatga 900
ctcttagcac tttgaaagaa aaaggctaca aagctgcttt cattggaata ggtttgccag 960
aacccaataa agatgccatc ttccaaggcc tgacgcagga ccaggggttt tatacatcca 1020
aagacttttt gccacttgta gccaaaggca gtaaagcagg aatgtgcgcc tgtcactctc 1080
cattgccatc gatacgggga gtcgtgattg tacttggagc tggagacact gccttcgact 1140
gtgcaacatc tgctctacgt tgtggagctc gccgagtgtt catcgtcttc agaaaaggct 1200
ttgttaatat aagagctgtc cctgaggaga tggagcttgc taaggaagaa aagtgtgaat 1260
ttctgccatt cctgtcccca cggaaggtta tagtaaaagg tgggagaatt gttgctatgc 1320
agtttgttcg gacagagcaa gatgaaactg gaaaatggaa tgaagatgaa gatcagatgg 1380
tccatctgaa agccgatgtg gtcatcagtg cctttggttc agttctgagt gatcctaaag 1440

taaaagaagc cttgagccct ataaaattta acagatgggg tctcccagaa gtagatccag 1500
aaactatgca aactagtgaa gcatgggtat ttgcaggtgg tgatgtcgtt ggtttggcta 1560
acactacagt ggaatcggtg aatgatggaa agcaagcttc ttggtacatt cacaaatacg 1620
tacagtcaca atatggagct tccgtttctg ccaagcctga actacccctc ttttacactc 1680
ctattgatct ggtggacatt agtgtagaaa tggccggatt gaagtttata aatccttttg 1740
gtcttgctag cgcaactcca gccaccagca catcaatgat tcgaagagct tttgaagctg 1800
gatgggggtt tgccctcacc aaaactttct ctcttgataa ggacattgtg acaaatgttt 1860
cccccagaat catccgggga accacctctg gccccatgta tggccctgga caaagctcct 1920
ttctgaatat tgagctcatc agtgagaaaa cggctgcata ttggtgtcaa agtgtcactg 1980
aactaaaggc tgacttccca gacaacattg tgattgctag cattatgtgc agttacaata 2040
aaaatgactg gacggaactt gccaagaagt ctgaggattc tggagcagat gccctggagt 2100
taaatttatc atgtccacat ggcatgggag aaagaggaat gggcctggcc tgtgggcagg 2160
atccagagct ggtgcggaac atctgccgct gggttaggca agctgttcag attccttttt 2220
ttgccaagct gaccccaaat gtcactgata ttgtgagcat cgcaagagct gcaaaggaag 2280
gtggtgccaa tggcgttaca gccaccaaca ctgtctcagg tctgatggga ttaaaatctg 2340
atggcacacc ttggccagca gtggggattg caaagcgaac tacatatgga ggagtgtctg 2400
ggacagcaat cagacctatt gctttgagag ctgtgacctc cattgctcgt gctctgcctg 2460
gatttcccat tttggctact ggtggaattg actctgctga aagtggtctt cagtttctcc 2520
atagtggtgc ttccgtcctc caggtatgca gtgccattca gaatcaggat ttcactgtga 2580
tcgaagacta ctgcactggc ctcaaagccc tgctttatct gaaaagcatt gaagaactac 2640
aagactggga tggacagagt ccagctactg tgagtcacca gaaagggaaa ccagttccac 2700
gtatagctga actcatggac aagaaactgc caagttttgg accttatctg gaacagcgca 2760
agaaaatcat agcagaaaac aagattagac tgaaagaaca aaatgtagct tttcaccac 2820
ttaagagaag ctgttttatc cccaaaaggc ctattcctac catcaaggat gtaataggaa 2880
aagcactgca gtaccttgga acatttggtg aattgagcaa cgtagagcaa gttgtggcta 2940
tgattgatga agaaatgtgt atcaactgtg gtaaatgcta catgacctgt aatgattctg 3000
gctaccaggc tatacagttt gatccagaaa cccacctgcc caccataacc gacacttgta 3060
caggctgtac tctgtgtctc agtgtttgcc ctattgtcga ctgcatcaaa atggtttcca 3120
ggacaacacc ttatgaacca aagagaggcg taccctttatc tgtgaatccg gtgtgttaag 3180
gtgatttgtg aaacagttgc tgtgaacttt catgtcacct acatatgctg atctcttaaa 3240
atcatgatcc ttgtgttcag ctctttccaa attaaaacaa atatacattt tctaaataaa 3300
aatatgtaat ttcaaaatac atttgtaagt gtaaaaaatg tctcatgtca atgaccattc 3360
aattagtggc ataaaataga ataattcttt tctgaggata gtagttaaat aactgtgtgg 3420
cagttaattg gatgttcact gccagttgtc ttatgtgaaa aattaacttt ttgtgtggca 3480
attagtgtga cagtttccaa attgccctat gctgtgctcc atatttgatt tctaattgta 3540
agtgaaatta agcattttga aacaaagtac tctttaacat acaagaaaat gtatccaagg 3600
aaacatttta tcaataaaaa ttacctttaa ttttaatgct gtttctaaga aaatgtagtt 3660
agctccataa agtacaaatg aagaaagtca aaaattattt gctatggcag gataagaaag 3720
cctaaaattg agtttgtgga ctttattaag taaaatcccc ttcgctgaaa ttgcttattt 3780
ttggtgttgg atagaggata gggagaatat ttactaacta aataccattc actactcatg 3840
cgtgagatgg gtgtacaaac tcatcctctt ttaatggcat ttctctttaa actatgttcc 3900
taaccaaatg agatgatagg atagatcctg gttaccactc ttttactgtg cacatatggg 3960
ccccggaatt ctttaatagt caccttcatg attatagcaa ctaatgtttg aacaaagctc 4020
aaagtatgca atgcttcatt attcaagaat gaaaaatata atgttgataa tatatattaa 4080
gtgtgccaaa tcagtttgac tactctctgt tttagtgttt atgtttaaaa gaaatatatt 4140
ttttgttatt attagataat atttttgtat ttctctattt tcataatcag taaatagtgt 4200
catataaact catttatctc ctcttcatgg catcttcaat atgaatctat aagtagtaaa 4260
tcagaaagta acaatctatg gcttatttct atgacaaatt caagagctag aaaaataaaa 4320
tgtttcatta tgcactttta gaaatgcata tttgccacaa aacctgtatt actgaataat 4380
atcaaataaa atatcataaa gcatttt 4407

<210> 300
<211> 5532
<212> DNA
<213> Homo sapiens

<400> 300
gccgcgctgc gccggagtcc cgagctagcc ccggcgccgc cgccgcccag accggacgac 60
aggccacctc gtcggcgtcc gcccgagtcc ccgcctcgcc gccaacgcca caaccaccgc 120
gcacggcccc ctgactccgt ccagtattga tcgggagagc cggagcgagc tcttcgggga 180
gcagcgatgc gaccctccgg gacggccggg gcagcgctcc tggcgctgct ggctgcgctc 240
tgcccggcga gtcgggctct ggaggaaaag aaagtttgcc aaggcacgag taacaagctc 300
acgcagttgg gcacttttga agatcatttt ctcagcctcc agaggatgtt caataactgt 360
gaggtggtcc ttgggaattt ggaaattacc tatgtgcaga ggaattatga tctttccttc 420
ttaaagacca tccaggaggt ggctggttat gtcctcattg ccctcaacac agtggagcga 480
attcctttgg aaaacctgca gatcatcaga ggaaatatgt actacgaaaa ttcctatgcc 540
ttagcagtct tatctaacta tgatgcaaat aaaaccggac tgaaggagct gcccatgaga 600
aatttacagg aaatcctgca tggcgccgtg cggttcagca acaaccctgc cctgtgcaac 660

```
gtggagagca tccagtggcg ggacatagtc agcagtgact ttctcagcaa catgtcgatg 720
gacttccaga accacctggg cagctgccaa aagtgtgatc caagctgtcc caatgggagc 780
tgctggggtg caggagagga gaactgccag aaactgacca aaatcatctg tgcccagcag 840
tgctccgggc gctgccgtgg caagtccccc agtgactgct gccacaacca gtgtgctgca 900
ggctgcacag gcccccggga gagcgactgc ctggtctgcc gcaaattccg agacgaagcc 960
acgtgcaagg acacctgccc cccactcatg ctctacaacc ccaccacgta ccagatggat 1020
gtgaaccccg agggcaaata cagctttggt gccacctgcg tgaagaagtg tccccgtaat 1080
tatgtggtga cagatcacgg ctcgtgcgtc cgagcctgtg gggccgacag ctatgagatg 1140
gaggaagacg gcgtccgcaa gtgtaagaag tgcgaagggc cttgccgcaa agtgtgtaac 1200
ggaataggta ttggtgaatt taaagactca ctctccataa atgctacgaa tattaaacac 1260
ttcaaaaact gcacctccat cagtggcgat ctccacatcc tgccggtggc atttaggggt 1320
gactccttca cacatactcc tcctctggat ccacaggaac tggatattct gaaaaccgta 1380
aaggaaatca cagggttttt gctgattcag gcttggcctg aaaacaggac ggacctccat 1440
gcctttgaga acctagaaat catacgcggc aggaccaagc aacatggtca gttttctctt 1500
gcagtcgtca gcctgaacat aacatccttg ggattacgct ccctcaagga gataagtgat 1560
ggagatgtga taatttcagg aaacaaaaat ttgtgctatg caaatacaat aaactggaaa 1620
aaactgtttg ggacctccgg tcagaaaacc aaaattataa gcaacagagg tgaaaacagc 1680
tgcaaggcca caggccaggt ctgccatgcc ttgtgctccc ccgagggctg ctggggcccg 1740
gagcccaggg actgcgtctc ttgccggaat gtcagccgag gcagggaatg cgtggacaag 1800
tgcaagcttc tggagggtga gccaagggag tttgtggaga actctgagtg catacagtgc 1860
cacccagagt gcctgcctca ggccatgaac atcacctgca caggacgggg accagacaac 1920
tgtatccagt gtgcccacta cattgacggc ccccactgcg tcaagacctg cccggcagga 1980
gtcatgggag aaaacaacac cctggtctgg aagtacgcag acgccggcca tgtgtgccac 2040
ctgtgccatc caaactgcac ctacggatgc actgggccag gtcttgaagg ctgtccaacg 2100
aatgggccta agatcccgtc catcgccact gggatggtgg gggccctcct cttgctgctg 2160
gtggtggccc tggggatcgg cctcttcatg cgaaggcgcc acatcgttcg gaagcgcacg 2220
ctgcggaggc tgctgcagga gagggagctt gtggagcctc ttacacccag tggagaagct 2280
cccaaccaag ctctcttgag gatcttgaag gaaactgaat tcaaaaagat caaagtgctg 2340
ggctccggtg cgttcggcac ggtgtataag ggactctgga tcccagaagg tgagaaagtt 2400
aaaattcccg tcgctatcaa ggaattaaga gaagcaacat ctccgaaagc caacaaggaa 2460
atcctcgatg aagcctacgt gatggccagc gtggacaacc cccacgtgtg ccgcctgctg 2520
ggcatctgcc tcacctccac cgtgcaactc atcacgcagc tcatgccctt cggctgcctc 2580
ctggactatg tccgggaaca caaagacaat attggctccc agtacctgct caactggtgt 2640
gtgcagatcg caaagggcat gaactacttg gaggaccgtc gcttggtgca ccgcgacctg 2700
gcagccagga acgtactggt gaaaacaccg cagcatgtca agatcacaga ttttgggctg 2760
gccaaactgc tgggtgcgga agagaaagaa taccatgcag aaggaggcaa agtgcctatc 2820
aagtggatgg cattggaatc aattttacac agaatctata cccaccagag tgatgtctgg 2880
agctacgggg tgaccgtttg ggagttgatg acctttggat ccaagccata tgacggaatc 2940
cctgccagcg agatctcctc catcctggag aaaggagaac gcctccctca gccacccata 3000
tgtaccatcg atgtctacat gatcatggtc aagtgctgga tgatagacgc agatagtcgc 3060
ccaaagttcc gtgagttgat catcgaattc tccaaaatgg cccgagaccc ccagcgctac 3120
cttgtcattc agggggatga aagaatgcat ttgccaagtc ctacagactc caacttctac 3180
cgtgccctga tggatgaaga agacatggac gacgtggtgg atgccgacga gtacctcatc 3240
ccacagcagg gcttcttcag cagcccctcc acgtcacgga ctcccctcct gagctctctg 3300
agtgcaacca gcaacaattc caccgtggct tgcattgata gaaatgggct gcaaagctgt 3360
cccatcaagg aagacagctt cttgcagcga tacagctcag accccacagg cgccttgact 3420
gaggacagca tagacgacac cttcctccca gtgcctgaat acataaacca gtccgttccc 3480
aaaaggcccg ctggctctgt gcagaatcct gtctatcaca atcagcctct gaaccccgcg 3540
cccagcagag acccacacta ccaggacccc cacagcactg cagtgggcaa ccccgagtat 3600
ctcaacactg tccagcccac ctgtgtcaac agcacattcg acagccctgc ccactgggcc 3660
cagaaaggca gccaccaaat tagcctggac aaccctgact accagcagga cttctttccc 3720
aaggaagcca agccaaatgg catctttaag ggctccacag ctgaaaatgc agaataccta 3780
agggtcgcgc cacaaagcag tgaatttatt ggagcatgac cacggaggat agtatgagcc 3840
ctaaaaatcc agactctttc gatacccagg accaagccac agcaggtcct ccatcccaac 3900
agccatgccc gcattagctc ttagacccac agactggttt tgcaacgttt acaccgacta 3960
gccaggaagt acttccacct cgggcacatt ttgggaagtt gcattccttt gtcttcaaac 4020
tgtgaagcat ttacagaaac gcatccagca agaatattgt ccctttgagc agaaatttat 4080
ctttcaaaga ggtatatttg aaaaaaaaaa aaaaagtata tgtgaggatt tttattgatt 4140
ggggatcttg gagtttttca ttgtcgctat tgatttttac ttcaatgggc tcttccaaca 4200
aggaagaagc ttgctggtag cacttgctac cctgagttca tccaggccca actgtgagca 4260
aggagcacaa gccacaagtc ttccagagga tgcttgattc cagtggttct gcttcaaggc 4320
ttccactgca aaacactaaa gatccaagaa ggccttcatg gccccagcag gccggatcgg 4380
tactgtatca agtcatggca ggtacagtag gataagccac tctgtccctt cctgggcaaa 4440
gaagaaacgg aggggatgaa ttcttcctta gacttacttt tgtaaaaatg tccccacggt 4500
acttactccc cactgatgga ccagtggttt ccagtcatga gcgttagact gacttgtttg 4560
tcttccattc cattgttttg aaactcagta tgccgcccct gtcttgctgt catgaaatca 4620
gcaagagagg atgacacatc aaataataac tcggattcca gcccacattg gattcatcag 4680
catttggacc aatagcccac agctgagaat gtggaatacc taaggataac accgcttttg 4740
```

```
ttctcgcaaa aacgtatctc ctaatttgag gctcagatga aatgcatcag gtcctttggg 4800
gcatagatca gaagactaca aaaatgaagc tgctctgaaa tctcctttag ccatcacccc 4860
aacccccaa aattagtttg tgttacttat ggaagatagt tttctccttt tacttcactt 4920
caaaagcttt ttactcaaag agtatatgtt ccctccaggt cagctgcccc caaacccccct 4980
ccttacgctt tgtcacacaa aaagtgtctc tgccttgagt catctattca agcacttaca 5040
gctctggcca caacagggca ttttacaggt gcgaatgaca gtagcattat gagtagtgtg 5100
aattcaggta gtaaatatga aactagggtt tgaaattgat aatgctttca caacatttgc 5160
agatgtttta gaaggaaaaa agttccttcc taaaataatt tctctacaat tggaagattg 5220
gaagattcag ctagttagga gcccattttt tcctaatctg tgtgtgccct gtaacctgac 5280
tggttaacag cagtcctttg taaacagtgt tttaaactct cctagtcaat atccaccccca 5340
tccaatttat caaggaagaa atggttcaga aaatattttc agcctacagt tatgttcagt 5400
cacacacaca tacaaaatgt tcctttgct tttaaagtaa tttttgactc ccagatcagt 5460
cagagcccct acagcattgt taagaaagta tttgattttt gtctcaatga aaataaaact 5520
atattcattt cc 5532
```

<210> 301
<211> 1528
<212> DNA
<213> Homo sapiens

<400> 301

```
cggcgagcga gcaccttcga cgcggtccgg ggacccctc gtcgctgtcc tcccgacgcg 60
gacccgcgtg ccccaggcct cgcgctgccc ggccggctcc tcgtgtccca ctcccggcgc 120
acgccctccc gcgagtcccg ggcccctccc gcgcccctct tctcggcgcg cgcgcagcat 180
ggcgcccccg caggtcctcg cgttcgggct tctgcttgcc gcggcgacgg cgacttttgc 240
cgcagctcag gaagaatgtg tctgtgaaaa ctacaagctg gccgtaaact gctttgtgaa 300
taataatcgt caatgccagt gtacttcagt tggtgcacaa aatactgtca tttgctcaaa 360
gctggctgcc aaatgtttgg tgatgaaggc agaaatgaat ggctcaaaac ttgggagaag 420
agcaaaacct gaaggggccc tccagaacaa tgatgggctt tatgatcctg actgcgatga 480
gagcgggctc tttaaggcca agcagtgcaa cggcacctcc acgtgctggt gtgtgaacac 540
tgctggggtc agaagaacag acaaggacac tgaaataacc tgctctgagc gagtgagaac 600
ctactggatc atcattgaac taaaacacaa agcaagagaa aaaccttatg atagtaaaag 660
tttgcggact gcacttcaga aggagatcac aacgcgttat caactggatc caaaatttat 720
cacgagtatt ttgtatgaga ataatgttat cactattgat ctggttcaaa attcttctca 780
aaaaactcag aatgatgtgg acatagctga tgtggcttat tattttgaaa aagatgttaa 840
aggtgaatcc ttgtttcatt ctaagaaaat ggacctgaca gtaaatgggg aacaactgga 900
tctggatcct ggtcaaactt taatttatta tgttgatgaa aaagcacctg aattctcaat 960
gcagggtcta aaagctggtg ttattgctgt tattgtggtt gtggtgatag cagttgttgc 1020
tggaattgtt gtgctggtta tttccagaaa gaagagaatg gcaaagtatg agaaggctga 1080
gataaaggag atgggtgaga tgcataggga actcaatgca taactatata atttgaagat 1140
tatagaagaa gggaaatagc aaatggacac aaattacaaa tgtgtgtgcg tgggacgaag 1200
acatctttga aggtcatgag tttgttagtt taacatcata tatttgtaat agtgaaacct 1260
gtactcaaaa tataagcagc ttgaaactgg ctttaccaat cttgaaattt gaccacaagt 1320
gtcttatata tgcagatcta atgtaaaatc cagaacttgg actccatcgt taaaattatt 1380
tatgtgtaac attcaaatgt gtgcattaaa tatgcttcca cagtaaaatc tgaaaaactg 1440
atttgtgatt gaaagctgcc tttctattta cttgagtctt gtacatacat actttttat 1500
gagctatgaa ataaaacatt ttaaactg 1528
```

<210> 302
<211> 1856
<212> DNA
<213> Homo sapiens

<400> 302

```
ctgacttggc aggactgtgc aattgtcaga aggccgtggg gagtgggggc cagtgcctgc 60
agcctgccct gcctctctca caggccctta gagcatcgcc aggtgcagag ctccacagct 120
ctctttccca aggagtaatc agagggtgag aacgtggagc ctggtggaca ggtgaaagca 180
ctgggatctt tctgcccaga aaggggaaag ttgcacattt atatcctaga gggaagcgac 240
agcagtgctt ctccctgtgc tgaggtacag gagccatgtg gctagaaatc ctcctcactt 300
cagtgctggg ctttgccatc tactggttca tctcccggga caaagaggaa actttgccac 360
ttgaagatgg gtggtgggg ccaggcacga ggtccgcagc cagggaggac gacagcatcc 420
gcccctttcaa ggtggaaacg tcagatgagg agatccacga cttacaccag aggatcgata 480
agttccgttt caccccacct ttggaggaca gctgcttcca ctatggcttc aactccaact 540
acctgaagaa agtcatctcc tactggcgga atgaatttga ctggaagaag caggtggaga 600
ttctcaacag ataccctcac ttcaagacta agattgaagg gctggacatc cacttcatcc 660
acgtgaagcc cccccagctg cccgcaggcc ataccccgaa gcccttgctg atggtgcacg 720
```

gctggcccgg ctctttctac gagttttata agatcatccc actcctgact gaccccaaga 780
accatggcct gagcgatgag cacgtttttg aagtcatctg cccttccatc cctggctatg 840
gcttctcaga ggcatcctcc aagaaggggt tcaactcggt ggccaccgcc aggatctttt 900
acaagctgat gctgcggctg ggcttccagg aattctacat tcaaggaggg gactggggggt 960
ccctgatctg cactaatatg gcccagctgg tgcccagcca cgtgaaaggc ctgcacttga 1020
acatggcttt ggttttaagc aacttctcta ccctgaccct cctcctggga cagcgtttcg 1080
ggaggtttct tggcctcact gagagggatg tggagctgct gtaccccgtc aaggagaagg 1140
tattctacag cctgatgagg gagagcggct acatgcacat ccagtgcacc aagcctgaca 1200
ccgtaggctc tgctctgaat gactctcctg tgggtctggc tgcctatatt ctagagaagt 1260
tttccacctg gaccaatacg gaattccgat acctggagga tggaggcctg gaaaggaagt 1320
tctccctgga cgacctgctg accaacgtca tgctctactg gacaacaggc accatcatct 1380
cctcccagcg cttctacaag gagaacctgg gacagggctg gatgacccag aagcatgagc 1440
ggatgaaggt ctatgtgccc actggcttct ctgccttccc ttttgagcta ttgcacacgc 1500
ctgaaaagtg ggtgaggttc aagtacccaa agctcatctc ctattcctac atggttcgtg 1560
ggggccactt tgcggccttt gaggagccgg agctgctcgc ccaggacatc cgcaagttcc 1620
tgtcggtgct ggagcggcaa tgacccaccc ctctcccccc gcctgccacc tccccccaca 1680
agtgccctcc aggcttttct tggggaagat accccttttc tgaggaatga gtttgcctcc 1740
gtcccctgcc catgctggga gcccacgctc acccccctcac ccctccaagc tcactcccca 1800
acccccaact ccgtgtggta agcaacatgg ctttgatgat aaacgacttt actcta 1856

<210> 303
<211> 6450
<212> DNA
<213> Homo sapiens

<400> 303
gagttgtgcc tggagtgatg tttaagccaa tgtcagggca aggcaacagt ccctggccgt 60
cctccagcac ctttgtaatg catatgagct cgggagacca gtacttaaag ttggaggccc 120
gggagcccag gagctggcgg agggcgttcg tcctgggagc tgcacttgct ccgtcgggtc 180
gccggcttca ccggaccgca ggctcccggg gcagggccgg ggccagagct cgcgtgtcgg 240
cgggacatgc gctgcgtcgc ctctaacctc gggctgtgct ctttttccag gtggcccgcc 300
ggtttctgag ccttctgccc tgcggggaca cggtctgcac cctgcccgcg gccacggacc 360
atgaccatga ccctccacac caaagcatct gggatggccc tactgcatca gatccaaggg 420
aacgagctgg agcccctgaa ccgtccgcag ctcaagatcc ccctggagcg gcccctgggc 480
gaggtgtacc tggacagcag caagcccgcc gtgtacaact accccgaggg cgccgcctac 540
gagttcaacg ccgcggccgc cgccaacgcg caggtctacg gtcagaccgg cctcccctac 600
ggccccgggt ctgaggctgc ggcgttcggc tccaacggcc tggggggttt ccccccactc 660
aacagcgtgt ctccgagccc gctgatgcta ctgcacccgc cgccgcagct gtcgcctttc 720
ctgcagcccc acggccagca ggtgccctac tacctggaga acgagcccag cggctacacg 780
gtgcgcgagg ccggcccgcc ggcattctac aggccaaatt cagataatcg acgccagggt 840
ggcagagaaa gattggccag taccaatgac aagggaagta tggctatgga atctgccaag 900
gagactcgct actgtgcagt gtgcaatgac tatgcttcag gctaccatta tggagtctgg 960
tcctgtgagg gctgcaaggc cttcttcaag agaagtattc aaggacataa cgactatatg 1020
tgtccagcca ccaaccagtg caccattgat aaaaacagga ggaagagctg ccaggcctgc 1080
cggctccgca aatgctacga agtgggaatg atgaaaggtg ggatacgaaa agaccgaaga 1140
ggagggagaa tgttgaaaca caagcgccag agagatgatg gggagggcag gggtgaagtg 1200
gggtctgctg gagacatgag agctgccaac ctttggccaa gcccgctcat gatcaaacgc 1260
tctaagaaga acagcctggc cttgtccctg acggccgacc agatggtcag tgccttgttg 1320
gatgctgagc cccccatact ctattccgag tatgatccta ccagaccctt cagtgaagct 1380
tcgatgatgg gcttactgac caacctggca gacagggagc tggttcacat gatcaactgg 1440
gcgaagaggg tgccaggctt tgtggatttg accctccatg atcaggtcca ccttctagaa 1500
tgtgcctggc tagagatcct gatgattggt ctcgtctggc gctccatgga gcacccagtg 1560
aagctactgt ttgctcctaa cttgctcttg gacaggaacc agggaaaatg tgtagagggc 1620
atggtggaga tcttcgacat gctgctggct acatcatctc ggttccgcat gatgaatctg 1680
cagggagagg agtttgtgtg cctcaaatct attattttgc ttaattctgg agtgtacaca 1740
tttctgtcca gcaccctgaa gtctctggaa gagaaggacc atatccaccg agtcctggac 1800
aagatcacag acactttgat ccacctgatg gccaaggcag gcctgaccct gcagcagcag 1860
caccagcggc tggcccagct cctcctcatc ctctcccaca tcaggcacat gagtaacaaa 1920
ggcatggagc atctgtacag catgaagtgc aagaacgtgg tgcccctcta tgacctgctg 1980
ctggagatgc tggacgccca ccgcctacat gcgcccacta gccgtggagg ggcatccgtg 2040
gaggagacgg accaaagcca cttggccact gcgggctcta cttcatcgca ttccttgcaa 2100
aagtattaca tcacggggga ggcagagggt ttccctgcca cagtctgaga gctccctggc 2160
tcccacacgg ttcagataat ccctgctgca ttttaccctc atcatgcacc actttagcca 2220
aattctgtct cctgcataca ctccggcatg catccaacac caatggcttt ctagatgagt 2280
ggccattcat ttgcttgctc agttcttagt ggcacatctt ctgtcttctg ttgggaacag 2340
ccaaagggat tccaaggcta aatctttgta acagctctct ttcccccttg ctatgttact 2400
aagcgtgagg attcccgtag ctcttcacag ctgaactcag tctatgggtt ggggctcaga 2460
taactctgtg catttaagct acttgtagag acccaggcct ggagagtaga cattttgcct 2520

```
ctgataagca ctttttaaat ggctctaaga ataagccaca gcaaagaatt taaagtggct 2580
cctttaattg gtgacttgga gaaagctagg tcaagggttt attatagcac cctcttgtat 2640
tcctatggca atgcatcctt ttatgaaagt ggtacacctt aaagctttta tatgactgta 2700
gcagagtatc tggtgattgt caattcactt cccctatag gaatacaagg ggccacacag 2760
ggaaggcaga tcccctagtt ggccaagact tattttaact tgatacactg cagattcaga 2820
gtgtcctgaa gctctgcctc tggctttccg gtcatgggtt ccagttaatt catgcctccc 2880
atggacctat ggagagcaac aagttgatct tagttaagtc tccctatatg agggataagt 2940
tcctgatttt tgtttttatt tttgtgttac aaaagaaagc cctccctccc tgaacttgca 3000
gtaaggtcag cttcaggacc tgttccagtg ggcactgtac ttggatcttc ccggcgtgtg 3060
tgtgccttac acaggggtga actgttcact gtggtgatgc atgatgaggg taaatggtag 3120
ttgaaaggag caggggccct ggtgttgcat ttagccctgg ggcatggagc tgaacagtac 3180
ttgtgcagga ttgttgtggc tactagagaa caagagggaa agtagggcag aaactggata 3240
cagttctgag cacagccaga cttgctcagg tggccctgca caggctgcag ctacctagga 3300
acattccttg cagaccccgc attgcctttg ggggtgccct gggatccctg gggtagtcca 3360
gctcttattc atttcccagc gtggccctgg ttggaagaag cagctgtcaa gttgtagaca 3420
gctgtgttcc tacaattggc ccagcacccct ggggcacggg agaagggtgg ggaccgttgc 3480
tgtcactact caggctgact ggggcctggt cagattacgt atgcccttgg tggtttagag 3540
ataatccaaa atcagggttt ggtttgggga agaaaatcct ccccccttcct cccccgcccc 3600
gttccctacc gcctccactc ctgccagctc atttccttca atttcctttg acctataggc 3660
taaaaaagaa aggctcattc cagccacagg gcagccttcc ctgggccttt gcttctctag 3720
cacaattatg ggttacttcc tttttcttaa caaaaaagaa tgtttgattt cctctgggtg 3780
accttattgt ctgtaattga aaccctattg agaggtgatg tctgtgttag ccaatgaccc 3840
aggtagctgc tcgggcttct cttggtatgt cttgtttgga aaagtggatt tcattcattt 3900
ctgattgtcc agttaagtga tcaccaaagg actgagaatc tgggagggca aaaaaaaaaa 3960
aaaaagtttt tatgtgcact taaatttggg gacaatttta tgtatctgtg ttaaggatat 4020
gcttaagaac ataattcttt tgttgctgtt tgtttaagaa gcaccttagt ttgtttaaga 4080
agcaccttat atagtataat atatattttt ttgaaattac attgcttgtt tatcagacaa 4140
ttgaatgtag taattctgtt ctggatttaa tttgactggg ttaacatgca aaaaccaagg 4200
aaaaatattt agtttttttt tttttttttg tatacttttc aagctacctt gtcatgtata 4260
cagtcattta tgcctaaagc ctggtgatta ttcatttaaa tgaagatcac atttcatatc 4320
aacttttgta tccacagtag acaaaatagc actaatccag atgcctattg ttggatattg 4380
aatgacagac aatcttatgt agcaaagatt atgcctgaaa aggaaaatta ttcagggcag 4440
ctaattttgc ttttaccaaa atatcagtag taatattttt ggacagtagc taatgggtca 4500
gtgggttctt tttaatgttt atacttagat tttcttttaa aaaaattaaa ataaaacaaa 4560
aaaaatttct aggactagac gatgtaatac cagctaaagc caaacaatta tacagtggaa 4620
ggtttacat tattcatcca atgtgtttct attcatgtta agatactact acatttgaag 4680
tgggcagaga acatcagatg attgaaatgt tcgcccaggg gtctccagca actttggaaa 4740
tctctttgta tttttacttg aagtgccact aatggacagc agatattttc tggctgatgt 4800
tggtattggg tgtaggaaca tgatttaaaa aaaaaactct tgcctctgct ttcccccact 4860
ctgaggcaag ttaaaatgta aaagatgtga tttatctggg gggctcaggt atggtgggga 4920
agtggattca ggaatctggg gaatggcaaa tatattaaga agagtattga aagtatttgg 4980
aggaaaatgg ttaattctgg gtgtgcacca aggttcagta gagtccactt ctgccctgga 5040
gaccacaaat caactagctc catttacagc catttctaaa atggcagctt cagttctaga 5100
gaagaaagaa caacatcagc agtaaagtcc atggaatagc tagtggtctg tgtttctttt 5160
cgccattgcc tagcttgccg taatgattct ataatgccat catgcagcaa ttatgagagg 5220
ctaggtcatc caaagagaag accctatcaa tgtaggttgc aaaatctaac ccctaaggaa 5280
gtgcagtctt tgatttgatt tccctagtaa ccttgcagat atgtttaacc aagccatagc 5340
ccatgccttt tgagggctga acaaataagg gacttactga taatttactt ttgatcacat 5400
taaggtgttc tcaccttgaa atcttataca ctgaaatggc cattgattta ggccactggc 5460
ttagagtact ccttcccctg catgacactg attacaaata ctttcctatt catactttcc 5520
aattatgaga tggactgtgg gtactgggag tgatcactaa caccatagta atgtctaata 5580
ttcacaggca gatctgcttg gggaagctag ttatgtgaaa ggcaaataaa gtcatacagt 5640
agctcaaaag gcaaccataa ttctctttgg tgcaagtctt gggagcgtga tctagattac 5700
actgcaccat tcccaagtta atcccctgaa aacttactct caactggagc aaatgaactt 5760
tggtcccaaa tatccatctt ttcagtagcg ttaattatgc tctgtttcca actgcatttc 5820
ctttccaatt gaattaaagt gtggcctcgt ttttagtcat ttaaaattgt tttctaagta 5880
attgctgcct ctattatggc acttcaattt tgcactgtct tttgagattc aagaaaaatt 5940
tctattcatt tttttgcatc caattgtgcc tgaactttta aaatatgtaa atgctgccat 6000
gttccaaacc catcgtcagt gtgtgtgttt agagctgtgc accctagaaa caacatactt 6060
gtcccatgag caggtgcctg agacacagac ccctttgcat tcacagagag gtcattggtt 6120
atagagactt gaattaataa gtgacattat gccagtttct gttctctcac aggtgataaa 6180
caatgctttt tgtgcactac atactcttca gtgtagagct cttgttttat gggaaaaggc 6240
tcaaatgcca aattgtgttt gatggattaa tatgcccttt tgccgatgca tactattact 6300
gatgtgactc ggttttgtcg cagctttgct ttgtttaatg aaacacactt gtaaacctct 6360
tttgcacttt gaaaaagaat ccagcgggat gctcgagcac ctgtaaacaa ttttctcaac 6420
ctatttgatg ttcaaataaa gaattaaact                                  6450
```

<210> 304
<211> 3336
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (0)...(0)
<223> n = A, T, C or G

<400> 304
cggcggcgac tgcagtctgg agggtccaca cttgtgattc tcaatggaga gtgaaaacgc 60
agattcataa tgaaagctag cccccgtcgg ccactgattc tcaaaagacg gaggctgccc 120
cttcctgttc aaaatgcccc aagtgaaaca tcagaggagg aacctaagag atcccctgcc 180
caacaggagt ctaatcaagc agaggcctcc aaggaagtgg cggagtccaa ctcttgcaag 240
tttccagctg ggatcaagat tattaaccac cccaccatgc ccaacacgca agtagtggcc 300
atccccaaca atgctaatat tcacagcatc atcacagcac tgactgccaa gggaaaagag 360
agtggcagta gtgggcccaa caaattcatc ctcatcagct gtgggggagc cccaactcag 420
cctccaggac tccggcctca aacccaaacc agctatgatg ccaaaaggac agaagtgacc 480
ctggagacct tgggaccaaa acctgcagct agggatgtga atcttcctag accacctgga 540
gcccttttgcg agcagaaacg ggagacctgt gcagatggtg aggcagcagg ctgcactatc 600
aacaatagcc tatccaacat ccagtggctt cgaaagatga gttctgatgg actgggctcc 660
cgcagcatca agcaagagat ggaggaaaag gagaattgtc acctggagca gcgacaggtt 720
aaggttgagg agccttcgag accatcagcg tcctggcaga actctgtgtc tgagcggcca 780
ccctactctt acatggccat gatacaattc gccatcaaca gcactgagag gaagcgcatg 840
actttgaaag acatctatac gtggattgag gaccactttc cctactttaa gcacattgcc 900
aagccaggct ggaagaactc catccgccac aacctttccc tgcacgacat gtttgtccgg 960
gagacgtctg ccaatggcaa ggtctccttc tggaccattc accccagtgc caaccgctac 1020
ttgacattgg accaggtgtt taagccactg gacccagggt ctccacaatt gcccgagcac 1080
ttggaatcac agcagaaacg accgaatcca gagctccgcc ggaacatgac catcaaaacc 1140
gaactccccc tgggcgcacg gcggaagatg aagccactgc taccacgggt cagctcatac 1200
ctggtaccta tccagttccc ggtgaaccag tcactggtgt tgcagccctc ggtgaaggtg 1260
ccattgcccc tggcggcttc cctcatgagc tcagagcttg cccgccatag caagcgagtc 1320
cgcattgccc ccaaggtgct gctagctgag gaggggatag ctcctctttc ttctgcagga 1380
ccagggaaag aggagaaact cctgtttgga gaagggtttt ctcctttgct tccagttcag 1440
actatcaagg aggaagaaat ccagcctggg gaggaaatgc cacacttagc gagacccatc 1500
aaagtggaga gccctccctt ggaagagtgg ccctccccgg ccccatcttt caaagaggaa 1560
tcatctcact cctgggagga ttcgtcccaa tctcccaccc caagacccaa gaagtcctac 1620
agtgggctta ggtccccaac ccggtgtgtc tcggaaatgc ttgtgattca acacagggag 1680
aggagggaga ggagccggtc tcggaggaaa cagcatctac tgcctccctg tgtggatgag 1740
ccggagctgc tcttctcaga ggggcccagt acttcccgct gggccgcaga gctcccgttc 1800
ccagcagact cctctgaccc tgcctcccag ctcagctact cccaggaagt gggaggacct 1860
tttaagacac ccattaagga aacgctgccc atctcctcca ccccgagcaa atctgtcctc 1920
cccagaaccc ctgaatcctg gaggctcacg cccccagcca aagtaggggg actggatttc 1980
agcccagtac aaacctccca gggtgcctct gaccccttgc ctgacccccct ggggctgatg 2040
gatctcagca ccactcccctt gcaaagtgct cccccccttg aatcaccgca aaggctcctc 2100
agttcagaac ccttagacct catctccgtc ccctttggca actcttctcc ctcagatata 2160
gacgtcccca agccaggctc cccggagcca caggtttctg gccttgcagc caatcgttct 2220
ctgacagaag gcctggtcct ggacacaatg aatgacagcc tcagcaagat cctgctggac 2280
atcagctttc ctggcctgga cgaggaccca ctgggccctg acaacatcaa ctggtcccag 2340
tttattcctg agctacagta gagccctgcc cttgcccctg tgctcaagct gtccaccatc 2400
ccgggcactc caaggctcag tgcaccccaa gcctctgagt gaggacagca ggcagggact 2460
gttctgctcc tcatagctcc ctgctgcctg attatgcaaa agtagcagtc acaccctagc 2520
cactgctggg accttgtgtt ccccaagagt atctgattcc tctgctgtcc ctgccaggag 2580
ctgaagggtg ggaacaacaa aggcaatggt gaaaagagat taggaacccc ccagcctgtt 2640
tccattctct gcccagcagt ctcttacctt ccctgatctt tgcagggtgg tccgtgtaaa 2700
tagtataaat tctccaaatt atcctctaat tataaatgta agcttatttc cttagatcat 2760
tatccagaga ctgccagaag gtgggtagga tgacctgggg tttcaattga cttctgttcc 2820
ttgcttttag ttttgataga agggaagacc tgcagtgcac ggtttcttcc aggctgaggt 2880
acctggatct tgggttcttc actgcaggga cccagacaag tggatctgct tgccagagtc 2940
ctttttgccc ctccctgcca cctccccgtg tttccaagtc agctttcctg caagaagaaa 3000
tcctggttaa aaaagtcttt tgtattgggt caggagttga atttggggtg ggaggatgga 3060
tgcaactgaa gcagagtgtg ggtgcccaga tgtgcgctat tagatgtttc tctgataatg 3120
tccccaatca taccagggag actggcattg acgagaactc aggtggaggc ttgagaaggc 3180
cgaaagggcc cctgacctgc ctggcttcct tagcttgccc ctcagctttg caaagagcca 3240
ccctaggccc cagctgaccg catgggtgtg agccagcttg agaacactaa ctactcaata 3300
aaagcgaagg tggaccnaaa aaaaaaaaaa aaaaaa 3336

<210> 305
<211> 2365
<212> DNA
<213> Homo sapiens

<400> 305
tcccagcctt cccatccccc caccgaaagc aaatcattca acgacccccg accctccgac 60
ggcaggagcc ccccgacctc ccaggcggac cgcccttccc tccccgcgcg ggttccgggc 120
ccggcgagag ggcgcgacga cagccgaggc catggaggtg acggcggacc agccgcgctg 180
ggtgagccac caccaccccg ccgtgctcaa cgggcagcac ccggacacgc accacccggg 240
cctcagccac tcctacatgg acgcggcgca gtacccgctg ccggaggagg tggatgtgct 300
ttttaacatc gacggtcaag gcaaccacgt cccgccctac tacggaaact cggtcagggc 360
cacggtgcag aggtaccctc cgacccacca cgggagccag gtgtgccgcc cgcctctgct 420
tcatggatcc ctaccctggc tggacggcgg caaagccctg ggcagccacc acaccgcctc 480
cccctggaat ctcagcccct tctccaagac gtccatccac cacggctccc cggggcccct 540
ctccgtctac cccccggcct cgtcctcctc cttgtcgggg ggccacgcca gcccgcacct 600
cttcaccttc ccgcccaccc cgccgaagga cgtctccccg gacccatcgc tgtccacccc 660
aggctcggcc ggctcggccc ggcaggacga gaaagagtgc ctcaagtacc aggtgcccct 720
gcccgacagc atgaagctgg agtcgtccca ctcccgtggc agcatgaccg ccctgggtgg 780
agcctcctcg tcgacccacc accccatcac cacctacccg ccctacgtgc ccgagtacag 840
ctccggactc ttcccccccca gcagcctgct gggcggctcc cccaccggct tcggatgcaa 900
gtccaggccc aaggcccggt ccagcacagg cagggagtgt gtgaactgtg ggcaacctc 960
gaccccactg tggcggcgag atggcacggg acactacctg tgcaacgcct gcgggctcta 1020
tcacaaaatg aacggacaga accggcccct cattaagccc aagcgaaggc tgtctgcagc 1080
caggagagca gggacgtcct gtgcgaactg tcagaccacc acaaccacac tctggaggag 1140
gaatgccaat ggggaccctg tctgcaatgc ctgtgggctc tactacaagc ttcacaatat 1200
taacagaccc ctgactatga agaaggaagg catccagacc agaaaccgaa aaatgtctag 1260
caaatccaaa aagtgcaaaa aagtgcatga ctcactggag gacttcccca agaacagctc 1320
gtttaacccg gccgccctct ccagacacat gtcctccctg agccacatct cgcccttcag 1380
ccactccagc cacatgctga ccacgcccac gccgatgcac ccgccatcca gcctgtcctt 1440
tggaccacac caccccctcca gcatggtcac cgccatgggt tagagccctg ctcgatgctc 1500
acagggcccc cagcgagagt ccctgcagtc cctttcgact tgcatttttg caggagcagt 1560
atcatgaagc ctaaacgcga tggatatatg tttttgaagg cagaaagcaa aattatgttt 1620
gccactttgc aaaggagctc actgtggtgt ctgtgttcca accactgaat ctggacccca 1680
tctgtgaata agccattctg actcatatcc cctatttaac agggtctcta gtgctgtgaa 1740
aaaaaaaaat cctgaacatt gcatataact tatattgtaa gaaatactgt acaatgactt 1800
tattgcatct gggtagctgt aaggcatgaa ggatgccaag aagtttaagg aatatgggag 1860
aaatagtgtg gaaattaaga agaaactagg tctgatattc aaatggacaa actgccagtt 1920
ttgtttcctt tcactggcca cagttgtttg atgcattaaa agaaaataaa aaaaagaaaa 1980
aagagaaaag aaaaaaaaag aaaaaagttg taggcgaatc atttgttcaa agctgttggc 2040
cctctgcaaa ggaaatacca gttctgggca atcagtgtta ccgttcacca gttgccattg 2100
agggtttcag agagcctttt tctaggccta catgctttgt gaacaagtcc ctgtaattgt 2160
tgtttgtatg tataattcaa agcaccaaaa taagaaaaga tgtagattta tttcatcata 2220
ttatacagac cgaactgttg tataaattta tttactgcta gtcttaagaa ctgctttctt 2280
tcgtttgttt gtttcaatat tttccttctc tctcaatttt cggttgaata aactagatta 2340
cattcagttg gcaaaaaaaa aaaaa 2365

<210> 306
<211> 1117
<212> DNA
<213> Homo sapiens

<400> 306
gcaccaacca gcaccatgcc catgatactg ggtactggg acatccgcgg gctggcccac 60
gccatccgcc tgctcctgga atacacagac tcaagctatg aggaaaagaa gtacacgatg 120
ggggacgctc ctgattatga cagaagccag tggctgaatg aaaaattcaa gctgggcctg 180
gactttccca atctgcccta cttgattgat ggggctcaca agatcaccca gagcaacgcc 240
atcttgtgct acattgcccg caagcacaac ctgtgtgggg agacagaaga ggagaagatt 300
cgtgtggaca ttttggagaa ccagaccatg gacaaccata tgcagctggg catgatctgc 360
tacaatccag aatttgagaa actgaagcca aagtacttgg aggaactccc tgaaaagcta 420
aagctctact cagagtttct ggggaagcgg ccatggtttg caggaaacaa gatcactttt 480
gtagattttc tcgtctatga tgtccttgac ctccaccgta tatttgagcc caactgcttg 540
gacgccttcc caaatctgaa ggacttcatc tcccgctttg agggcttgga gaagatctct 600
gcctacatga agtccagccg cttcctccca agacctgtgt tctcaaagat ggctgtctgg 660
ggcaacaagt agggccttga aggcaggagg tgggagtgag gagcccatac tcagcctgct 720
gcccaggctg tgcagcgcag ctggactctg catcccagca cctgcctcct cgttcctttc 780
tcctgtttat tcccatcttt actcccaaga cttcattgtc cctcttcact ccccctaaac 840

39740-0001PCT.txt
ccctgtccca tgcaggccct ttgaagcctc agctacccac tatccttcgt gaacatcccc 900
tcccatcatt acccttccct gcactaaagc cagcctgacc ttccttcctg ttagtggttg 960
tgtctgcttt aaagcctgcc tggcccctcg cctgtggagc tcagccccga gctgtccccg 1020
tgttgcatga aggagcagca ttgactggtt tacaggccct gctcctgcag catggtccct 1080
gcctaggcct acctgatgga agtaaagcct caaccac 1117

<210> 307
<211> 1266
<212> DNA
<213> Homo sapiens

<400> 307
ctcggaagcc cgtcaccatg tcgtgcgagt cgtctatggt tctcgggtac tgggatattc 60
gtgggctggc gcacgccatc cgcctgctcc tggagttcac ggatacctct tatgaggaga 120
aacggtacac gtgcggggaa gctcctgact atgatcgaag ccaatggctg gatgtgaaat 180
tcaagctaga cctggacttt cctaatctgc cctacctcct ggatgggaag aacaagatca 240
cccagagcaa tgccatcttg cgctacatcg ctcgcaagca caacatgtgt ggtgagactg 300
aagaagaaaa gattcgagtg gacatcatag agaaccaagt aatggatttc cgcacacaac 360
tgataaggct ctgttacagc tctgaccacg aaaaactgaa gcctcagtac ttggaagagc 420
tacctggaca actgaaacaa ttctccatgt ttctgtggaa attctcatgg tttgccgggg 480
aaaagctcac ctttgtggat ttttctcacct atgatatctt ggatcagaac cgtatatttg 540
accccaagtg cctggatgag ttcccaaacc tgaaggcttt catgtgccgt tttgaggctt 600
tggagaaaat cgctgcctac ttacagtctg atcagttctg caagatgccc atcaacaaca 660
agatggccca gtggggcaac aagcctgtat gctgagcagg aggcagactt gcagagcttg 720
ttttgtttca tcctgtccgt aaggggtcag cgctcttgct ttgctctttt caatgaatag 780
cacttatgtt actggtgtcc agctgagttt ctcttgggta taaaggctaa aagggaaaaa 840
ggatatgtgg agaatcatca agatatgaat tgaatcgctg cgatactgtg gcatttccct 900
actccccaac tgagttcaag ggctgtaggt tcatgcccaa gccctgagag tgggtactag 960
aaaaaacgag attgcacagt tggagagagc aggtgtgtta aatggactgg agtccctgtg 1020
aagactgggt gaggataaca caagtaaaac tgtggtactg atggacttaa ccggagttcg 1080
gaaaccgtcc tgtgtacaca tgggagttta gtgtgataaa ggcagtattt cagactggtg 1140
ggctagccaa tagagttggc aattgcttat tgaaactcat taaaaataat agagccccac 1200
ttgacactat tcactaaaat taatctggaa tttaaggccc aacattaaac acaaagctgt 1260
attgat 1266

<210> 308
<211> 2162
<212> DNA
<213> Homo sapiens

<400> 308
gggctgcgct gtccagctgt ggctatggcc ccagccccga gatgaggagg gagagaacta 60
ggggcccgca ggcctgggaa tttccgtccc ccaccaagtc cggatgctca ctccaaagtc 120
tcagcaggcc cctgagggag ggagctgtca gccagggaaa accgagaaca ccatcaccat 180
gacaaccagt caccagcctc aggacagata caaagctgtc tggcttatct tcttcatgct 240
gggtctggga acgctgctcc cgtggaattt tttcatgacg gccactcagt atttcacaaa 300
ccgcctggac atgtcccaga atgtgtcctt ggtcactgct gaactgagca aggacgccca 360
ggcgtcagcc gcccctgcag caccccttgcc tgagcggaac tctctcagtg ccatcttcaa 420
caatgtcatg accctatgtg ccatgctgcc cctgctgtta ttcacctacc tcaactcctt 480
cctgcatcag aggatccccc agtccgtacg gatcctgggc agcctggtgg ccatcctgct 540
ggtgtttctg atcactgcca tcctggtgaa ggtgcagctg gatgctctgc ccttctttgt 600
catcaccatg atcaagatcg tgctcattaa ttcatttggt gccatcctgc agggcagcct 660
gtttggtctg gctggccttc tgcctgccag ctacacggcc cccatcatga gtggccaggg 720
cctagcaggc ttctttgcct ccgtggccat gatctgcgct attgccagtg gctcggaact 780
atcagaaagt gccttcggct actttatcac agcctgtgct gttatcattt tgaccatcat 840
ctgttacctg ggcctgcccc gcctggaatt ctaccgctac taccagcagc tcaagcttga 900
aggacccggg gagcaggaga ccaagttgga cctcattagc aaaggagagg agccaagagc 960
aggcaaagag gaatctggag tttcagtctc caactctcag cccaccaatg aaagccactc 1020
tatcaaagcc atcctgaaaa atatctcagt cctggctttc tctgtctgct tcatcttcac 1080
tatcaccatt gggatgtttc cagccgtgac tgttgaggtc aagtccagca tcgcaggcag 1140
cagcacctgg gaacgttact tcattcctgt gtcctgtttc ttgactttca atatctttga 1200
ctggttgggc cggagcctca cagctgtatt catgtggcct gggaaggaca gccgctggct 1260
gccaagcctg gtgctggccc ggctggtgtt tgtgccactg ctgctgctgt gcaacattaa 1320
gccccgccgc tacctgactg tggtcttcga gcacgatgcc tggttcatct tcttcatggc 1380
tgcctttgcc ttctccaacg gctacctcgc cagcctctgc atgtgcttcg ggcccaagaa 1440
agtgaagcca gctgaggcag agaccgcagg agccatcatg gccttcttcc tgtgtctggg 1500
tctggcactg gggctgttt tctccttcct gttccgggca attgtgtgac aaaggatgga 1560
cagaaggact gcctgcctcc ctccctgtct gcctcctgcc ccttccttct gccaggggtg 1620

atcctgagtg gtctggcggt tttttcttct aactgacttc tgctttccac ggcgtgtgct 1680
gggcccggat ctccaggccc tggggaggga gcctctggac ggacagtggg gacattgtgg 1740
gtttggggct cagagtcgag ggacggggtg tagcctcggc atttgcttga gtttctccac 1800
tcttggctct gactgatccc tgcttgtgca ggccagtgga ggctcttggg cttggagaac 1860
acgtgtgtct ctgtgtatgt gtctgtgtgt ctgcgtccgt gtctgtcaga ctgtctgcct 1920
gtcctggggt ggctaggagc tgggtctgac cgttgtatgg tttgacctga tatactccat 1980
tctcccctgc gcctcctcct ctgtgttttt tccatgtccc cctcccaact ccccatgccc 2040
agtttttacc catcatgcac cctgtacagt tgccacgtta ctgccttttt taaaaatata 2100
tttgacagaa accaggtgcc ttcagaggct ctctgattta aataaacctt tcttgttttt 2160
tt 2162

<210> 309
<211> 3933
<212> DNA
<213> Homo sapiens

<400> 309
cacgaggcag cactctcttc gtcgcttcgg ccagtgtgtc gggctgggcc ctgacaagcc 60
acctgaggag aggctcggag ccgggcccgg accccggcga ttgccgcccg cttctctcta 120
gtctcacgag gggtttcccg cctcgcaccc ccacctctgg acttgccttt ccttctcttc 180
tccgcgtgtg gagggagcca gcgcttaggc cggagcgagc ctgggggccg cccgccgtga 240
agacatcgcg gggaccgatt caccatggag ggcgccggcg gcgcgaacga caagaaaaag 300
ataagttctg aacgtcgaaa agaaaagtct cgagatgcag ccagatctcg gcgaagtaaa 360
gaatctgaag tttttatga gcttgctcat cagttgccac ttccacataa tgtgagttcg 420
catcttgata aggcctctgt gatgaggctt accatcagct atttgcgtgt gaggaaactt 480
ctggatgctg gtgatttgga tattgaagat gacatgaaag cacagatgaa ttgcttttat 540
ttgaaagcct tggatggttt tgttatggtt ctcacagatg atggtgacat gatttacatt 600
tctgataatg tgaacaaata catgggatta actcagtttg aactaactgg acacagtgtg 660
tttgatttta ctcatccatg tgaccatgag gaaatgagag aaatgcttac acacagaaat 720
ggccttgtga aaaagggtaa agaacaaaac acacagcgaa gcttttttct cagaatgaag 780
tgtaccctaa ctagccgagg aagaactatg aacataaagt ctgcaacatg gaaggtattg 840
cactgcacag gccacattca cgtatatgat accaacagta accaacctca gtgtgggtat 900
aagaaaccac ctatgacctg cttggtgctg atttgtgaac ccattcctca cccatcaaat 960
attgaaattc ctttagatag caagactttc ctcagtcgac acagcctgga tatgaaattt 1020
tcttattgtg atgaaagaat taccgaattg atgggatatg agccagaaga acttttaggc 1080
cgctcaattt atgaatatta tcatgctttg gactctgatc atctgaccaa aactcatcat 1140
gatatgttta ctaaaggaca agtcaccaca ggacagtaca ggatgcttgc caaaagaggt 1200
ggatatgtct gggttgaaac tcaagcaact gtcatatata acaccaagaa ttctcaacca 1260
cagtgcattg tatgtgtgaa ttacgttgtg agtggtatta ttcagcacga cttgattttc 1320
tcccttcaac aaacagaatg tgtccttaaa ccggttgaat cttcagatat gaaaatgact 1380
cagctattca ccaaagttga atcagaagat acaagtagcc tctttgacaa acttaagaag 1440
gaacctgatg ctttaacttt gctggcccca gccgctggag acacaatcat atctttagat 1500
tttggcagca acgacacaga aactgatgac cagcaacttg aggaagtacc attatataat 1560
gatgtaatgc tcccctcacc caacgaaaaa ttacagaata taaatttggc aatgtctcca 1620
ttacccaccg ctgaaacgcc aaagccactt cgaagtagtg ctgaccctgc actcaatcaa 1680
gaagttgcat taaaattaga accaaatcca gagtcactgg aactttcttt taccatgccc 1740
cagattcagg atcagacacc tagtccttcc gatggaagca ctagacaaag ttcacctgag 1800
cctaatagtc ccagtgaata ttgtttttat gtggatagtg atatggtcaa tgaattcaag 1860
ttggaattgg tagaaaaact ttttgctgaa gacacagaag caaagaaccc attttctact 1920
caggacacag atttagactt ggagatgtta gctccctata tcccaatgga tgatgacttc 1980
cagttacgtt ccttcgatca gttgtcacca ttagaaagca gttccgcaag ccctgaaagc 2040
gcaagtcctc aaagcacagt tacagtattc cagcagactc aaatacaaga acctactgct 2100
aatgccacca ctaccactgc caccactgat gaattaaaaa cagtgacaaa agaccgtatg 2160
gaagacatta aaatattgat tgcatctcca tctcctaccc acatacataa agaaactact 2220
agtgccacat catcaccata tagagatact caaagtcgga cagcctcacc aaacagagca 2280
ggaaaaggag tcatagaaca gacagaaaaa tctcatccaa gaagccctaa cgtgttatct 2340
gtcgctttga gtcaaagaac tacagttcct gaggaagaac taaatccaaa gatactagct 2400
ttgcagaatg ctcagagaaa gcgaaaaatg gaacatgatg gttcactttt tcaagcagta 2460
ggaattggaa cattattaca gcagccagac gatcatgcag ctactacatc actttcttgg 2520
aaacgtgtaa aaggatgcaa atctagtgaa cagaatggaa tggagcaaaa gacaattatt 2580
ttaataccct ctgatttagc atgtagactg ctggggcaat caatggatga aagtggatta 2640
ccacagctga ccagttatga ttgtgaagtt aatgctccta tacaaggcag cagaaaccta 2700
ctgcagggtg aagaattact cagagctttg gatcaagtta actgagcttt ttcttaattt 2760
cattcctttt tttggacact ggtggctcac tacctaaagc agtctattta tattttctac 2820
atctaatttt agaagcctgg ctacaatact gcacaaactt ggttagttca atttttgatc 2880
ccctttctac ttaatttaca ttaatgctct tttttagtat gttctttaat gctggatcac 2940
agacagctca ttttctcagt tttttggtat ttaaaccatt gcattgcagt agcatcattt 3000
taaaaaatgc accttttat ttatttattt ttggctaggg agtttatccc tttttcgaat 3060

```
tatttttaag aagatgccaa tataattttt gtaagaaggc agtaaccttt catcatgatc 3120
ataggcagtt gaaaaatttt tacacctttt ttttcacatt ttacataaat aataatgctt 3180
tgccagcagt acgtggtagc cacaattgca caatatattt tcttaaaaaa taccagcagt 3240
tactcatgga atatattctg cgtttataaa actagttttt aagaagaaat tttttttggc 3300
ctatgaaatt gttaaacctg gaacatgaca ttgttaatca tataataatg attcttaaat 3360
gctgtatggt ttattattta aatgggtaaa gccatttaca taatatagaa agatatgcat 3420
atatctagaa ggtatgtggc atttatttgg ataaaattct caattcagag aaatcatctg 3480
atgtttctat agtcactttg ccagctcaaa agaaaacaat accctatgta gttgtggaag 3540
tttatgctaa tattgtgtaa ctgatattaa acctaaatgt tctgcctacc ctgttggtat 3600
aaagatattt tgagcagact gtaaacaaga aaaaaaaaat catgcattct tagcaaaatt 3660
gcctagtatg ttaatttgct caaaatacaa tgtttgattt tatgcacttt gtcgctatta 3720
acatcctttt tttcatgtag atttcaataa ttgagtaatt ttagaagcat tattttagga 3780
atatatagtt gtcacagtaa atatcttgtt ttttctatgt acattgtaca aatttttcat 3840
tccttttgct ctttgtggtt ggatctaaca ctaactgtat tgttttgtta catcaaataa 3900
acatcttctg tggaaaaaaa aaaaaaaaaa aaa                              3933

<210> 310
<211> 2872
<212> DNA
<213> Homo sapiens

<400> 310
tccaggaatc gatagtgcat tcgtgcgcgc ggccgcccgt cgcttcgcac agggctggat 60
ggttgtattg ggcagggtgg ctccaggatg ttaggaactg tgaagatgga agggcatgaa 120
accagcgact ggaacagcta ctacgcagac acgcaggagg cctactcctc ggtcccggtc 180
agcaacatga actcaggcct gggctccatg aactccatga acacctacat gaccatgaac 240
accatgacta cgagcggcaa catgaccccg gcgtccttca acatgtccta tgccaacccg 300
gccttagggg ccggcctgag tcccggcgca gtagccggca tgccgggggg ctcggcgggc 360
gccatgaaca gcatgactgc ggccggcgtg acggccatgg gtacggcgct gagcccgagc 420
ggcatgggcg ccatgggtgc gcagcaggcg gcctccatga tgaatggcct gggcccctac 480
gcggccgcca tgaacccgtg catgagcccc atggcgtacg cgccgtccaa cctgggccgc 540
agccgcgcgg gcggcggcgg cgacgccaag acgttcaagc gcagttaccc gcacgccaag 600
ccgccctact cgtacatctc gctcatcacc atggccatcc agcgggcgcc cagcaagatg 660
ctcacgctga gcgagatcta ccagtggatc atggacctct tcccctatta ccggcagaac 720
cagcagcgct ggcagaactc catccgccac tcgctgtcct tcaatgactg cttcgtcaag 780
gtggcacgct ccccggacaa gccgggcaag ggctcctact ggacgctgca cccggactcc 840
ggcaacatgt tcgagaacgg ctgctacttg cgccgccaga agcgcttcaa gtgcgagaag 900
cagccggggg ccggcggcgg gggcgggagc ggaagcgggg gcagcggcgc caagggcggc 960
cctgagagcc gcaaggaccc ctctggcgcc tctaacccca gcgccgactc gcccctccat 1020
cggggtgtgc acgggaagac cggccagcta gagggcgcgc cggcccgggg cccggccgcc 1080
agcccccaga ctctggacca cagtggggcg acggcgacag gggcgcctc ggagttgaag 1140
actccagcct cctcaactgc gccccccata agctccgggc ccggggcgct ggcctctgtg 1200
cccgcctctc acccggcaca cggcttggca ccccacgagt cccagctgca cctgaaaggg 1260
gacccccact actccttcaa ccacccgttc tccatcaaca acctcatgtc ctcctcggag 1320
cagcagcata agctggactt caaggcatac gaacaggcac tgcaatactc gccttacggc 1380
tctacgttgc ccgccagcct gcctctaggc agcgcctcgg tgaccaccag gagccccatc 1440
gagccctcag ccctggagcc ggcgtactac caaggtgtgt attccagacc cgtcctaaac 1500
acttcctagc tcccgggact ggggggtttg tctggcatag ccatgctggt agcaagagag 1560
aaaaaatcaa cagcaaacaa aaccacacaa accaaaccgt caacagcata ataaaatcca 1620
acaactattt ttatttcatt tttcatgcac aaccttgccc ccagtgcaaa agactgttac 1680
tttattattg tattcaaaat tcattgtgta tattactaca aagacggccc caaaccaatt 1740
tttttcctgc gaagtttaat gatccacaag tgtatatatg aaattctcct ccttccttgc 1800
ccccctctct ttcttccctc ttggccctcc agacattcta gtttgtggag ggttatttaa 1860
aaaacaaaaa ggaagatggt caagtttgta aaatatttgt ttgtgctttt ccccccctcct 1920
tacctgaccc cctacgagtt tacaggcttg tggcaatact cttaaccata agaattgaaa 1980
tggtgaagaa acaagtatac actagaggct cttaaaagta ttgaaaagac aatactgctg 2040
ttatatagca agacataaac agattataaa catcagagcc atttgcttct cagtttacat 2100
ttctgataca tgcagatagc agatgtcttt aaatgaaata catgtatatt gtgtatggac 2160
ttaattatgc acatgctcag atgtgtagac atcctccgta tatttacata acatatagag 2220
gtaatagata ggtgatatac gtgatacgtt ctcaagagtt gcttgaccga aagttacaag 2280
gaccccaacc cctttgctct ctacccacag atggccctgg gaacaatcct caggaattgc 2340
cctcaagaac tcgcttcttt gctttgagag tgccatggtc atgtcattct gaggtacata 2400
acacataaat tagtttctat gagtgtatac catttaaaga ttttttcagt aaagggaata 2460
ttacatgttg ggaggaggag ataagttata gggagctgga tttcaaacgg tggtccaaga 2520
ttcaaaaatc ctattgatag tggccatttt aatcattgcc atcgtgtgct tgtttcatcc 2580
agtgttatgc actttccaca gttggtgtta gtatagccag agggtttcat tattatttct 2640
ctttgctttc tcaatgttaa tttattgcat ggtttattct ttttctttac agctgaaatt 2700
gctttaaatg atggttaaaa ttacaaatta aattgggaat ttttatcaat gtgattgtaa 2760
```

ttaaaaatat tttgatttaa ataacaaaaa taataccaga ttttaagccg cggaaaatgt 2820
tcttgatcat ttgcagttaa ggactttaaa taaatcaaat gttaacaaaa aa 2872

<210> 311
<211> 926
<212> DNA
<213> Homo sapiens

<400> 311
ggggcccatt ctgtttcagc cagtcgccaa gaatcatgaa agtcgccagt ggcagcaccg 60
ccaccgccgc cgcgggcccc agctgcgcgc tgaaggccgg caagacagcg agcggtgcgg 120
gcgaggtggt gcgctgtctg tctgagcaga gcgtggccat ctcgcgctgc cggggcgccg 180
gggcgcgcct gcctgccctg ctggacgagc agcaggtaaa cgtgctgctc tacgacatga 240
acggctgtta ctcacgcctc aaggagctgg tgcccacccct gccccagaac cgcaaggtga 300
gcaaggtgga gattctccag cacgtcatcg actacatcag ggaccttcag ttggagctga 360
actcggaatc cgaagttggg acccccgggg gccgagggct gccggtccgg gctccgctca 420
gcaccctcaa cggcgagatc agcgccctga cggccgaggc ggcatgcgtt cctgcggacg 480
atcgcatctt gtgtcgctga agcgcctccc ccagggaccg gcggacccca gccatccagg 540
gggcaagagg aattacgtgc tctgtgggtc tcccccaacg cgcctcgccg gatctgaggg 600
agaacaagac cgatcggcgg ccactgcgcc cttaactgca tccagcctgg ggctgaggct 660
gaggcactgg cgaggagagg gcgctcctct ctgcacacct actagtcacc agagacttta 720
gggggtggga ttccactcgt gtgtttctat tttttgaaaa gcagacattt taaaaaatgg 780
tcacgtttgg tgcttctcag atttctgagg aaattgcttt gtattgtata ttacaatgat 840
caccgactga gaatattgtt ttacaatagt tctgtggggc tgttttttttg ttattaaaca 900
aataatttag atggtgaaaa aaaaaa 926

<210> 312
<211> 4989
<212> DNA
<213> Homo sapiens

<400> 312
tttttttttt ttttgagaaa gggaatttca tcccaaataa aaggaatgaa gtctggctcc 60
ggaggagggt ccccgacctc gctgtggggg ctcctgtttc tctccgccgc gctctcgctc 120
tggccgacga gtggagaaat ctgcgggcca ggcatcgaca tccgcaacga ctatcagcag 180
ctgaagcgcc tggagaactg cacggtgatc gagggctacc tccacatcct gctcatctcc 240
aaggccgagg actaccgcag ctaccgcttc cccaagctca cggtcattac cgagtacttg 300
ctgctgttcc gagtggctgg cctcgagagc ctcggagacc tcttccccaa cctcacggtc 360
atccgcggct ggaaactctt ctacaactac gccctggtca tcttcgagat gaccaatctc 420
aaggatattg ggctttacaa cctgaggaac attactcggg gggccatcag gattgagaaa 480
aatgctgacc tctgttacct ctccactgtg gactggtccc tgatcctgga tgcggtgtcc 540
aataactaca ttgtggggaa taagcccccca aaggaatgtg gggacctgtg tccagggacc 600
atggaggaga agccgatgtg tgagaagacc accatcaaca atgagtacaa ctaccgctgc 660
tggaccacaa accgctgcca gaaaatgtgc ccaagcacgt gtgggaagcg ggcgtgcacc 720
gagaacaatg agtgctgcca ccccgagtgc ctgggcagct gcagcgcgcc tgacaacgac 780
acggcctgtg tagcttgccg ccactactac tatgccggtg tctgtgtgcc tgcctgcccg 840
cccaacacct acaggtttga gggctggcgc tgtgtggacc gtgacttctg cgccaacatc 900
ctcagcgccg agagcagcga ctccgagggg tttgtgatcc acgacggcga gtgcatgcag 960
gagtgcccct cgggcttcat ccgcaacggc agccagagca tgtactgcat cccttgtgaa 1020
ggtccttgcc cgaaggtctg tgaggaagaa aagaaaacaa agaccattga ttctgttact 1080
tctgctcaga tgctccaagg atgcaccatc ttcaagggca atttgctcat taacatccga 1140
cgggggaata acattgcttc agagctggag aacttcatgg ggctcatcga ggtggtgacg 1200
ggctacgtga agatccgcca ttctcatgcc ttggtctcct tgtccttcct aaaaaacctt 1260
cgcctcatcc taggagagga gcagctagaa gggaattact ccttctacgt cctcgacaac 1320
cagaacttgc agcaactgtg ggactgggac caccgcaacc tgaccatcaa agcagggaaa 1380
atgtactttg ctttcaatcc caaattatgt gtttccgaaa tttaccgcat ggaggaagtg 1440
acggggacta aagggcgcca aagcaaaggg gacataaaca ccaggaacaa cggggagaga 1500
gcctcctgtg aaagtgacgt cctgcatttc acctccacca ccacgtcgaa gaatcgcatc 1560
atcataacct ggcaccggta ccggcccccct gactacaggg atctcatcag cttcaccgtt 1620
tactacaagg aagcaccctt taagaatgtc acagagtatg atgggcagga tgcctgcggc 1680
tccaacagct ggaacatggt ggacgtggac ctcccgccca acaaggacgt ggagcccggc 1740
atcttactac atgggctgaa gccctggact cagtacgccg tttacgtcaa ggctgtgacc 1800
ctcaccatgg tggagaacga ccatatccgt ggggccaaga gtgagatctt gtacattcgc 1860
accaatgctt cagttccttc cattcccttg gacgttcttt cagcatcgaa ctcctcttct 1920
cagttaatcg tgaagtggaa ccctccctct ctgcccaacg gcaacctgag ttactacatt 1980
gtgcgctggc agcggcagcc tcaggacggc tacctttacc ggcacaatta ctgctccaaa 2040
gacaaaatcc ccatcaggaa gtatgccgac ggcaccatcg acattgagga ggtcacagag 2100
aaccccaaga ctgaggtgtg tggtggggag aaagggcctt gctgcgcctg ccccaaaact 2160

39740-0001PCT.txt
gaagccgaga agcaggccga gaaggaggag gctgaatacc gcaaagtctt tgagaatttc 2220
ctgcacaact ccatcttcgt gcccagacct gaaaggaagc ggagagatgt catgcaagtg 2280
gccaacacca ccatgtccag ccgaagcagg aacaccacgg ccgcagacac ctacaacatc 2340
accgacccgg aagagctgga gacagagtac cctttctttg agagcagagt ggataacaag 2400
gagagaactg tcatttctaa ccttcggcct ttcacattgt accgcatcga tatccacagc 2460
tgcaaccacg aggctgagaa gctgggctgc agcgcctcca acttcgtctt tgcaaggact 2520
atgcccgcag aaggagcaga tgacattcct gggccagtga cctgggagcc aaggcctgaa 2580
aactccatct ttttaaagtg gccggaacct gagaatccca atggattgat tctaatgtat 2640
gaaataaaat acggatcaca agttgaggat cagcgagaat gtgtgtccag acaggaatac 2700
aggaagtatg gaggggccaa gctaaaccgg ctaaacccgg ggaactacac agcccggatt 2760
caggccacat ctctctctgg gaatgggtcg tggacagatc ctgtgttctt ctatgtccag 2820
gccaaaacag gatatgaaaa cttcatccat ctgatcatcg ctctgcccgt cgctgtcctg 2880
ttgatcgtgg gagggttggt gattatgctg tacgtcttcc atagaaagag aaataacagc 2940
aggctgggga atggagtgct gtatgcctct gtgaacccgg agtacttcag cgctgctgat 3000
gtgtacgttc ctgatgagtg ggaggtggct cgggagaaga tcaccatgag ccgggaactt 3060
gggcaggggt cgtttgggat ggtctatgaa ggagttgcca agggtgtggt gaaagatgaa 3120
cctgaaacca gagtggccat taaaacagtg aacgaggccg caagcatgcg tgagaggatt 3180
gagtttctca acgaagcttc tgtgatgaag gagttcaatt gtcaccatgt ggtgcgattg 3240
ctgggtgtgg tgtcccaagg ccagccaaca ctggtcatca tggaactgat gacacggggc 3300
gatctcaaaa gttatctccg gtctctgagg ccagaaatgg agaataatcc agtcctagca 3360
cctccaagcc tgagcaagat gattcagatg gccggagaga ttgcagacgg catggcatac 3420
ctcaacgcca ataagttcgt ccacagagac cttgctgccc ggaattgcat ggtagccgaa 3480
gatttcacag tcaaaatcgg agattttggt atgacgcgag atatctatga gacagactat 3540
taccggaaag gaggcaaagg gctgctgccc gtgcgctgga tgtctcctga gtccctcaag 3600
gatggagtct tcaccactta ctcggacgtc tggtccttcg ggtcgtcct ctgggagatc 3660
gccacactgg ccgagcagcc ctaccagggc ttgtccaacg agcaagtcct tcgcttcgtc 3720
atggagggcg gccttctgga caagccagac aactgtcctg acatgctgtt tgaactgatg 3780
cgcatgtgct ggcagtataa ccccaagatg aggccttcct tcctggagat catcagcagc 3840
atcaaagagg agatggagcc tggcttccgg gaggtctcct tctactacag cgaggagaac 3900
aagctgcccg agccggagga gctggacctg gagccagaga acatggagag cgtccccctg 3960
gacccctcgg cctcctcgtc ctccctgcca ctgcccgaca gacactcagg acacaaggcc 4020
gagaacggcc ccggccctgg ggtgctggtc ctccgcgcca gcttcgacga gagacagcct 4080
tacgcccaca tgaacggggg ccgcaagaac gagcgggcct tgccgctgcc ccagtcttcg 4140
acctgctgat ccttggatcc tgaatctgtg caaacagtaa cgtgtgcgca cgcgcagcgg 4200
ggtggggggg gagagagagt tttaacaatc cattcacaag cctcctgtac ctcagtggat 4260
cttcagttct gcccttgctg cccgcgggag acagcttctc tgcagtaaaa cacatttggg 4320
atgttccttt tttcaatatg caagcagctt tttattccct gcccaaaccc ttaactgaca 4380
tgggccttta agaaccttaa tgacaacact taatagcaac agagcacttg agaaccagtc 4440
tcctcactct gtccctgtcc ttccctgttc tccctttctc tctcctctct gcttcataac 4500
ggaaaaataa ttgccacaag tccagctggg aagccctttt tatcagtttg aggaagtggc 4560
tgtccctgtg gccccatcca accactgtac acacccgcct gacaccgtgg gtcattacaa 4620
aaaaacacgt ggagatggaa atttttacct ttatctttca cctttctagg gacatgaaat 4680
ttacaaaggg ccatcgttca tccaaggctg ttaccatttt aacgctgcct aattttgcca 4740
aaatcctgaa ctttctccct catcggcccg gcgctgattc ctcgtgtccg gaggcatggg 4800
tgagcatggc agctggttgc tccatttgag agacacgctg gcgacacact ccgtccatcc 4860
gactgcccct gctgtgctgc tcaaggccac aggcacacag gtctcattgc ttctgactag 4920
attattattt gggggaactg gacacaatag gtctttctct cagtgaaggt ggggagaagc 4980
tgaaccggc 4989

<210> 313
<211> 12515
<212> DNA
<213> Homo sapiens

<400> 313
ctaccgggcg gaggtgagcg cggcgccggc tcctcctgcg gcggactttg ggtgcgactt 60
gacgagcggt ggttcgacaa gtggccttgc gggccggatc gtcccagtgg aagagttgta 120
aatttgcttc tggccttccc ctacggatta tacctggcct tcccctacgg attatactca 180
acttactgtt tagaaaatgt ggcccacgag acgcctggtt actatcaaaa ggagcggggt 240
cgacggtccc cactttcccc tgagcctcag cacctgcttg tttggaaggg gtattgaatg 300
tgacatccgt atccagcttc ctgttgtgtc aaaacaacat tgcaaaattg aaatccatga 360
gcaggaggca atattacata atttcagttc cacaaatcca acacaagtaa atgggtctgt 420
tattgatgag cctgtacggc taaaacatgg agatgtaata actattattg atcgttcctt 480
caggtatgaa aatgaaagtc ttcagaatgg aaggaagtca actgaatttc caagaaaaat 540
acgtgaacag gagccagcac gtcgtgtctc aagatctagc ttctcttctg accctgatga 600
gaaagctcaa gattccaagg cctattcaaa aatcactgaa ggaaaagttt caggaaatcc 660
tcaggtacat atcaagaatg tcaaagaaga cagtaccgca gatgactcaa aagacagtgt 720
tgctcaggga acaactaatg ttcattcctc agaacatgct ggacgtaatg gcagaaatgc 780

39740-0001PCT.txt

agctgatccc atttctgggg attttaaaga aatttccagc gttaaattag tgagccgtta 840
tggagaattg aagtctgttc ccactacaca atgtcttgac aatagcaaaa aaaatgaatc 900
tccctttgg aagctttatg agtcagtgaa gaaagagttg gatgtaaaat cacaaaaaga 960
aaatgtccta cagtattgta gaaaatctgg attacaaact gattacgcaa cagagaaaga 1020
aagtgctgat ggtttacagg gggagaccca actgttggtc tcgcgtaagt caagaccaaa 1080
atctggtggg agcggccacg ctgtggcaga gcctgcttca cctgaacaag agcttgacca 1140
gaacaagggg aagggaagag acgtggagtc tgttcagact cccagcaagg ctgtgggcgc 1200
cagctttcct ctctatgagc cggctaaaat gaagacccct gtacaatatt cacagcaaca 1260
aaattctcca caaaaacata agaacaaaga cctgtatact actggtagaa gagaatctgt 1320
gaatctgggt aaaagtgaag gcttcaaggc tggtgataaa actcttactc ccaggaagct 1380
ttcaactaga aatcgaacac cagctaaagt tgaagatgca gctgactctg ccactaagcc 1440
agaaaatctc tcttccaaaa ccagaggaag tattcctaca gatgtggaag ttctgcctac 1500
ggaaactgaa attcacaatg agccattttt aactctgtgg ctcactcaag ttgagaggaa 1560
gatccaaaag gattccctca gcaagcctga gaaattgggc actacagctg gacagatgtg 1620
ctctgggtta cctggtctta gttcagttga tatcaacaac tttggtgatt ccattaatga 1680
gagtgaggga ataccttga aaagaaggcg tgtgtccttt ggtgggcacc taagacctga 1740
actatttgat gaaaacttgc ctcctaatac gcctctcaaa aggggagaag ccccaaccaa 1800
aagaaagtct ctggtaatgc acactccacc tgtcctgaag aaaatcatca aggaacagcc 1860
tcaaccatca ggaaaacaag agtcaggttc agaaatccat gtggaagtga aggcacaaag 1920
cttggttata agccctccag ctcctagtcc taggaaaact ccagttgcca gtgatcaacg 1980
ccgtaggtcc tgcaaaacag cccctgcttc cagcagcaaa tctcagacag aggttcctaa 2040
gagaggagga gaaagagtgg caacctgcct tcaaaagaga gtgtctatca gccgaagtca 2100
acatgatatt ttacagatga tatgttccaa aagaagaagt ggtgcttcgg aagcaaatct 2160
gattgttgca aaatcatggg cagatgtagt aaaacttggt gcaaaacaaa cacaaactaa 2220
agtcataaaa catggtcctc aaaggtcaat gaacaaaagg caaagaagac ctgctactcc 2280
aaagaagcct gtgggcgaag ttcacagtca atttagtaca ggccacgcaa actctccttg 2340
taccataata atagggaaag ctcatactga aaaagtacat gtgcctgctc gaccctacag 2400
agtgctcaac aacttcattt ccaaccaaaa aatggacttt aaggaagatc tttcaggaat 2460
agctgaaatg ttcaagaccc cagtgaagga gcaaccgcag ttgacaagca catgtcacat 2520
cgctatttca aattcagaga atttgcttgg aaaacagttt caaggaactg attcaggaga 2580
agaacctctg ctccccacct cagagagttt tggaggaaat gtgttcttca gtgcacagaa 2640
tgcagcaaaa cagccatctg ataaatgctc tgcaagccct cccttaagac ggcagtgtat 2700
tagagaaaat ggaaacgtag caaaaacgcc caggaacacc tacaaaatga cttctctgga 2760
gacaaaaact tcagatactg agacagagcc ttcaaaaaca gtatccactg taaacaggtc 2820
aggaaggtct acagagttca ggaatataca gaagctacct gtggaaagta agagtgaaga 2880
aacaaataca gaaattgttg agtgcatcct aaaaagaggt cagaaggcaa cactactaca 2940
acaaaggaga gaaggagaga tgaaggaaat agaaagacct tttgagacat ataaggaaaa 3000
tattgaatta aaagaaaacg atgaaaagat gaaagcaatg aagagatcaa gaacttgggg 3060
gcagaaatgt gcaccaatgt ctgacctgac agacctcaag agcttgcctg atacagaact 3120
catgaaagac acggcacgtg gccagaatct cctccaaacc caagatcatg ccaaggcacc 3180
aaagagtgag aaaggcaaaa tcactaaaat gccctgccag tcattacaac cagaaccaat 3240
aaacacccca acacacacaa aacaacagtt gaaggcatcc ctggggaaag taggtgtgaa 3300
agaagagctc ctagcagtcg gcaagttcac acggacgtca ggggagacca cgcacacgca 3360
cagagagcca gcaggagatg gcaagagcat cagaacgttt aaggagtctc caaagcagat 3420
cctggaccca gcagcccgtg taactggaat gaagaagtgg ccaagaacgc ctaaggaaga 3480
ggcccagtca ctagaagacc tggctggctt caaagagctc ttccagacac caggtccctc 3540
tgaggaatca atgactgatg agaaaactac caaaatagcc tgcaaatctc caccaccaga 3600
atcagtggac actccaacaa gcacaaagca atggcctaag agaagtctca ggaaagcaga 3660
tgtagaggaa gaattcttag cactcaggaa actaacacca tcagcaggga aagccatgct 3720
tacgcccaaa ccagcaggag gtgatgagaa agacattaaa gcatttatgg gaactccagt 3780
gcagaaactg gacctggcag gaactttacc tggcagcaaa agacagctac agactcctaa 3840
ggaaaaggcc caggctctag aagacctggc tggctttaaa gagctcttcc agactcctgg 3900
tcacaccgag gaattagtgg ctgctggtaa aaccactaaa ataccctgcg actctccaca 3960
gtcagaccca gtggacaccc caacaagcac aaagcaacga cccaagagaa gtatcaggaa 4020
agcagatgta gagggagaac tcttagcgtg caggaatcta atgccatcag caggcaaagc 4080
catgcacacg cctaaaccat cagtaggtga agagaaagac atcatcatat ttgtgggaac 4140
tccagtgcag aaactggacc tgacagagaa cttaaccggc agcaagagac ggccacaaac 4200
tcctaaggaa gaggcccagg ctctggaaga cctgactggc tttaaagagc tcttccagac 4260
ccctggtcat actgaagaag cagtggctgc tggcaaaact actaaaatgc cctgcgaatc 4320
ttctccacca gaatcagcag acaccccaac aagcacaaga aggcagccca agacaccttt 4380
ggagaaaagg gacgtacaga aggagctctc agccctgaag aagctcacac agacatcagg 4440
ggaaaccaca cacacagata aagtaccagg aggtgaggat aaaagcatca acgcgtttag 4500
ggaaactgca aaacagaaac tggacccagc agcaagtgta actggtagca agaggcaccc 4560
aaaaactaag gaaaaggccc aacccctaga agacctggct ggctggaaag agctcttcca 4620
gacaccagta tgcactgaca agcccacgac tcacgagaaa actaccaaaa tagcctgcag 4680
atcacaacca gacccagtgg acacaccaac aagctccaag ccacagtcca agagaagtct 4740
caggaaagtg gacgtagaag aagaattctt cgcactcagg aaacgaacac catcagcagg 4800
caaagccatg cacacaccca aaccagcagt aagtggtgag aaaaacatct acgcatttat 4860

gggaactcca gtgcagaaac tggacctgac agagaactta actggcagca agagacggct 4920
acaaactcct aaggaaaagg cccaggctct agaagacctg gctggcttta aagagctctt 4980
ccagacacga ggtcacactg aggaatcaat gactaacgat aaaactgcca aagtagcctg 5040
caaatcttca caaccagacc tagacaaaaa cccagcaagc tccaagcgac ggctcaagac 5100
atccctgggg aaagtgggcg tgaaagaaga gctcctagca gttggcaagc tcacacagac 5160
atcaggagag actacacaca cacacacaga gccaacagga gatggtaaga gcatgaaagc 5220
atttatggag tctccaaagc agatcttaga ctcagcagca agtctaactg gcagcaagag 5280
gcagctgaga actcctaagg gaaagtctga agtccctgaa gacctggccg gcttcatcga 5340
gctcttccag acaccaagtc acactaagga atcaatgact aatgaaaaaa ctaccaaagt 5400
atcctacaga gcttcacagc cagacctagt ggacacccca acaagctcca agccacagcc 5460
caagagaagt ctcaggaaag cagacactga agaagaattt ttagcattta ggaaacaaac 5520
gccatcagca ggcaaagcca tgcacacacc caaaccagca gtaggtgaag agaaagacat 5580
caacacgttt ttgggaactc cagtgcagaa actggaccag ccaggaaatt tacctggcag 5640
caatagacgg ctacaaactc gtaaggaaaa ggcccaggct ctagaagaac tgactggctt 5700
cagagagctt ttccagacac catgcactga taaccccaca gctgatgaga aaactaccaa 5760
aaaaatactc tgcaaatctc cgcaatcaga cccagcggac accccaacaa acacaaagca 5820
acggcccaag agaagcctca agaaagcaga cgtagaggaa gaatttttag cattcaggaa 5880
actaacacca tcagcaggca aagccatgca cacgcctaaa gcagcagtag gtgaagagaa 5940
agacatcaac acatttgtgg ggactccagt ggagaaactg gacctgctag gaaatttacc 6000
tggcagcaag agacggccac aaactcctaa agaaaaggcc aaggctctag aagatctggc 6060
tggcttcaaa gagctcttcc agacaccagg tcacactgag gaatcaatga ccgatgacaa 6120
aatcacagaa gtatcctgca aatctccaca accagaccca gtcaaaaccc caacaagctc 6180
caagcaacga ctcaagatat ccttggggaa agtaggtgtg aaagaagagg tcctaccagt 6240
cggcaagctc acacagacgt cagggaagac cacacagaca cacagagaga cagcaggaga 6300
tggaaagagc atcaaagcgt ttaaggaatc tgcaaagcag atgctggacc cagcaaacta 6360
tggaactggg atggagaggt ggccaagaac acctaaggaa gaggcccaat cactagaaga 6420
cctggccggc ttcaaagagc tcttccagac accagaccac actgaggaat caacaactga 6480
tgacaaaact accaaaatag cctgcaaatc tccaccacca gaatcaatgg acactccaac 6540
aagcacaagg aggcggccca aaacaccttt ggggaaaagg gatatagtgg aagagctctc 6600
agccctgaag cagctcacac agaccacaca cacagacaaa gtaccaggag atgaggataa 6660
aggcatcaac gtgttcaggg aaactgcaaa acagaaactg gacccagcag caagtgtaac 6720
tggtagcaag aggcagccaa gaactcctaa gggaaaagcc caacccctag aagacttggc 6780
tggcttgaaa gagctcttcc agacaccagt atgcactgac aagcccacga ctcacgagaa 6840
aactaccaaa atagcctgca gatctccaca accagaccca gtgggtaccc caacaatctt 6900
caagccacag tccaagagaa gtctcaggaa agcagacgta gaggaagaat ccttagcact 6960
caggaaacga acaccatcag tagggaaagc tatggacaca cccaaaccag caggaggtga 7020
tgagaaagac atgaaagcat ttatgggaac tccagtgcag aaattggacc tgccaggaaa 7080
tttacctggc agcaaaagat ggccacaaac tcctaaggaa aaggcccagg ctctagaaga 7140
cctggctggc ttcaaagagc tcttccagac accaggcact gacaagccca cgactgatga 7200
gaaaactacc aaaatagcct gcaaatctcc acaaccagac ccagtggaca ccccagcaag 7260
cacaaagcaa cggcccaaga gaaacctcag gaaagcagac gtagaggaag aatttttagc 7320
actcaggaaa cgaacaccat cagcaggcaa agccatggac accccaaaac cagcagtaag 7380
tgatgagaaa aatatcaaca catttgtgga aactccagtg cagaaactgg acctgctagg 7440
aaatttacct ggcagcaaga gacagccaca gactcctaag gaaaaggctg aggctctaga 7500
ggacctggtt ggcttcaaag aactcttcca gacaccaggt cacactgagg aatcaatgac 7560
tgatgacaaa atcacagaag tatcctgtaa atctccacag ccagagtcat tcaaaacctc 7620
aagaagctcc aagcaaaggc tcaagatacc cctggtgaaa gtggacatga aagaagagcc 7680
cctagcagtc agcaagctca cacggacatc aggggagact acgcaaacac acacagagcc 7740
aacaggagat agtaagagca tcaaagcgtt taaggagtct ccaaagcaga tcctggaccc 7800
agcagcaagt gtaactggta gcaggaggca gctgagaact cgtaaggaaa aggcccgtgc 7860
tctagaagac ctggttgact tcaaagagct cttctcagca ccaggtcaca ctgaagagtc 7920
aatgactatt gacaaaaaca caaaaattcc ctgcaaatct cccccaccag aactaacaga 7980
cactgccacg agcacaaaga gatgccccaa gacacgtccc aggaaagaag taaaagagga 8040
gctctcagca gttgagaggc tcacgcaaac atcagggcaa agcacacaca cacacaaaga 8100
accagcaagc ggtgatgagg gcatcaaagt attgaagcaa cgtgcaaaga agaaaccaaa 8160
cccagtagaa gaggaaccca gcaggagaag gccaagagca cctaaggaaa aggcccaacc 8220
cctggaagac ctggccggct tcacagagct ctctgaaaca tcaggtcaca ctcaggaatc 8280
actgactgct ggcaaagcca ctaaaatacc ctgcgaatct cccccactag aagtggtaga 8340
caccacagca agcacaaaga ggcatctcag gacacgtgtg cagaaggtac aagtaaaaga 8400
agagccttca gcagtcaagt tcacacaaac atcaggggaa accacggatg cagacaaaga 8460
accagcaggt gaagataaag gcatcaaagc attgaaggaa tctgcaaaac agacaccggc 8520
tccagcagca agtgtaactg gcagcaggag acggccaaga gcacccaggg aaagtgccca 8580
agccatagaa gacctagctg gcttcaaaga cccagcagca ggtcacactg aagaatcaat 8640
gactgatgac aaaaccacta aaataccctg caaatcatca ccagaactag aagacaccgc 8700
aacaagctca aagagacggc ccaggacacg tgcccagaaa gtagaagtga aggaggagct 8760
gttagcagtt ggcaagctca cacaaacctc aggggagacc acgcacaccg acaaagagcc 8820
ggtaggtgag ggcaaaggca cgaaagcatt taagcaacct gcaaagcgga acgtggacgc 8880
agaagatgta attggcagca ggagacagcc aagagcacct aaggaaaagg cccaacccct 8940

39740-0001PCT.txt

```
ggaagacctg gccagcttcc aagagctctc tcaaacacca ggccacactg aggaactggc 9000
aaatggtgct gctgatagct ttacaagcgc tccaaagcaa acacctgaca gtggaaaacc 9060
tctaaaaata tccagaagag ttcttcgggc ccctaaagta gaacccgtgg gagacgtggt 9120
aagcaccaga gaccctgtaa aatcacaaag caaaagcaac acttccctgc ccccactgcc 9180
cttcaagagg ggaggtggca aagatggaag cgtcacggga accaagaggc tgcgctgcat 9240
gccagcacca gaggaaattg tggaggagct gccagccagc aagaagcaga gggttgctcc 9300
cagggcaaga ggcaaatcat ccgaacccgt ggtcatcatg aagagaagtt tgaggacttc 9360
tgcaaaaaga attgaacctg cggaagagct gaacagcaac gacatgaaaa ccaacaaaga 9420
ggaacacaaa ttacaagact cggtccctga aaataaggga atatccctgc gctccagacg 9480
ccaagataag actgaggcag aacagcaaat aactgaggtc tttgtattag cagaaagaat 9540
agaaataaac agaaatgaaa agaagcccat gaagacctcc ccagagatgg acattcagaa 9600
tccagatgat ggagcccgga aacccatacc tagagacaaa gtcactgaga acaaaaggtg 9660
cttgaggtct gctagacaga atgagagctc ccagcctaag gtggcagagg agagcggagg 9720
gcagaagagt gcgaaggttc tcatgcagaa tcagaaaggg aaaggagaag caggaaattc 9780
agactccatg tgcctgagat caagaaagac aaaaagccag cctgcagcaa gcactttgga 9840
gagcaaatct gtgcagagag taacgcggag tgtcaagagg tgtgcagaaa atccaaagaa 9900
ggctgaggac aatgtgtgtg tcaagaaaat aacaaccaga agtcataggg acagtgaaga 9960
tatttgacag aaaaatcgaa ctgggaaaaa tataataaag ttagttttgt gataagttct 10020
agtgcagttt ttgtcataaa ttacaagtga attctgtaag taaggctgtc agtctgctta 10080
agggaagaaa actttggatt tgctgggtct gaatcggctt cataaactcc actgggagca 10140
ctgctgggct cctggactga gaatagttga acaccggggg ctttgtgaag gagtctgggc 10200
caaggtttgc cctcagcttt gcagaatgaa gccttgaggt ctgtcaccac ccacagccac 10260
cctacagcag ccttaactgt gacacttgcc acactgtgtc gtcgtttgtt tgcctatgtt 10320
ctccagggca cggtggcagg aacaactatc ctcgtctgtc ccaacactga gcaggcactc 10380
ggtaaacacg aatgaatgga taagcgcacg gatgaatgga gcttacaaga tctgtctttc 10440
caatggccgg gggcatttgg tccccaaatt aaggctattg gacatctgca caggacagtc 10500
ctatttttga tgtcctttcc tttctgaaaa taaagttttg tgctttggag aatgactcgt 10560
gagcacatct ttagggacca agagtgactt tctgtaagga gtgactcgtg gcttgccttg 10620
gtctcttggg aatacttttc taactagggt tgctctcacc tgagacattc tccacccgcg 10680
gaatctcagg gtcccaggct gtgggccatc acgacctcaa actggctcct aatctccagc 10740
tttcctgtca ttgaaagctt cggaagttta ctggctctgc tcccgcctgt tttctttctg 10800
actctatctg gcagcccgat gccacccagt acaggaagtg acaccagtac tctgtaaagc 10860
atcatcatcc ttggagagac tgagcactca gcaccttcag ccacgatttc aggatcgctt 10920
ccttgtgagc cgctgcctcc gaaatctcct ttgaagccca gacatctttc tccagcttca 10980
gacttgtaga tataactcgt tcatcttcat ttactttcca ctttgccccc tgtcctctct 11040
gtgttcccca aatcagagaa tagcccgcca tcccccagat cacctgtctg gattcctccc 11100
cattcaccca ccttgccagg tgcaggtgag gatggtgcac cagacagggt agctgtcccc 11160
caaaatgtgc cctgtgcggg cagtgccctg tctccacgtt tgtttcccca gtgtctggcg 11220
gggagccagg tgacatcata aatacttgct gaatgaatgc agaaatcagc ggtactgact 11280
tgtactatat tggctgccat gatagggttc tcacagcgtc atccatgatc gtaagggaga 11340
atgacattct gcttgaggga gggaatagaa aggggcaggg aggggacatc tgagggcttc 11400
acagggctgc aaagggtaca gggattgcac cagggcagaa caggggaggg tgttcaagga 11460
agagtggctc ttagcagagg cactttggaa ggtgtgaggc ataaatgctt ccttctacgt 11520
aggccaacct caaaactttc agtaggaatg ttgctatgat caagttgttc taacacttta 11580
gacttagtag taattatgaa cctcacatag aaaaatttca tccagccata tgcctgtgga 11640
gtggaatatt ctgtttagta gaaaaatcct ttagagttca gctctaacca gaaatcttgc 11700
tgaagtatgt cagcaccttt tctcaccctg gtaagtacag tatttcaaga gcacgctaag 11760
ggtggttttc attttacagg gctgttgatg atgggttaaa aatgttcatt taagggctac 11820
ccccgtgttt aatagatgaa caccacttct acacaaccct ccttggtact gggggaggga 11880
gagatctgac aaatactgcc cattccccta ggctgactgg atttgagaac aaatacccac 11940
ccatttccac catggtatgg taacttctct gagcttcagt ttccaagtga atttccatgt 12000
aataggacat tcccattaaa tacaagctgt ttttactttt tcgcctccca gggcctgtgc 12060
gatctggtcc cccagcctct cttgggcttt cttacactaa ctctgtacct accatctcct 12120
gcctccctta ggcaggcacc tccaaccacc acacactccc tgctgttttc cctgcctgga 12180
actttcccac cagccccacc aagatcattt catccagtcc tgagctcagc ttaagggagg 12240
cttcttgcct gtgggttccc tcacccccat gcctgtcctc caggctgggg caggttctta 12300
gtttgcctgg aattgttctg tacctctttg tagcacgtag tgttgtgaaa ctaagccact 12360
aattgagttt ctggctcccc tcctggggtt gtaagttttg ttcattcatg agggccgact 12420
gtatttcctg gttactgtat cccagtgacc agccacagga gatgtccaat aaagtatgtg 12480
atgaaatggt cttaaaaaaa aaaaaaaaaa aaaaa                            12515
```

<210> 314
<211> 2444
<212> DNA
<213> Homo sapiens

<400> 314
ggcacgaggc ggggccgggt cgcagctggg cccgcggcat ggacgaactg ttccccctca 60
tcttcccggc agagcagccc aagcagcggg gcatgcgctt ccgctacaag tgcgaggggc 120
gctccgcggg cagcatccca ggcgagagga gcacagatac caccaagacc caccccacca 180
tcaagatcaa tggctacaca ggaccaggga cagtgcgcat ctccctggtc accaaggacc 240
ctcctcaccg gcctcacccc cacgagcttg taggaaagga ctgccgggat ggcttctatg 300
aggctgagct ctgcccggac cgctgcatcc acagtttcca gaacctggga atccagtgtg 360
tgaagaagcg ggacctggag caggctatca gtcagcgcat ccagaccaac aacaacccct 420
tccaagttcc tatagaagag cagcgtgggg actacgacct gaatgctgtg cggctctgct 480
tccaggtgac agtgcgggac ccatcaggca ggcccctccg cctgccgcct gtcctttctc 540
atcccatctt tgacaatcgt gcccccaaca ctgccgagct caagatctgc cgagtgaacc 600
gaaactctgg cagctgcctc ggtggggatg agatcttcct actgtgtgac aaggtgcaga 660
aagaggacat tgaggtgtat ttcacgggac caggctggga ggcccgaggc tcctttcgc 720
aagctgatgt gcaccgacaa gtggccattg tgttccggac cctccctac gcagacccca 780
gcctgcaggc tcctgtgcgt gtctccatgc agctgcggcg gccttccgac cgggagctca 840
gtgagcccat ggaattccag tacctgccag atacagacga tcgtcaccgg attgaggaga 900
aacgtaaaag gacatatgag accttcaaga gcatcatgaa gaagagtcct ttcagcggac 960
ccaccgaccc ccggcctcca cctcgacgca ttgctgtgcc ttcccgcagc tcagcttctg 1020
tccccaagcc agcaccccag ccctatccct ttacgtcatc cctgagcacc atcaactatg 1080
atgagtttcc caccatggtg tttccttctg ggcagatcag ccaggcctcg gccttggccc 1140
cggcccctcc ccaagtcctg ccccaggctc cagcccctgc ccctgctcca gccatggtat 1200
cagctctggc ccaggcccca gcccctgtcc cagtcctagc cccaggccct cctcaggctg 1260
tggccccacc tgcccccaag cccacccagg ctggggaagg aacgctgtca gaggccctgc 1320
tgcagctgca gtttgatgat gaagacctgg gggccttgct tggcaacagc acagacccag 1380
ctgtgttcac agacctggca tccgtcgaca actccgagtt tcagcagctg ctgaaccagg 1440
gcatacctgt ggcccccac acaactgagc ccatgctgat ggagtaccct gaggctataa 1500
ctcgcctagt gacagcccag aggccccccg acccagctcc tgctccactg gggggccccgg 1560
ggctccccaa tggcctcctt tcaggagatg aagacttctc ctccattgcg gacatggact 1620
tctcagccct gctgagtcag atcagctcct aagggggtga cgcctgccct ccccagagca 1680
ctggttgcag gggattgaag ccctccaaaa gcacttacgg attctggtgg ggtgtgttcc 1740
aactgccccc aactttgtgg atgtcttcct tggagggggg agccatattt tattctttta 1800
ttgtcagtat ctgtatctct ctctcttttt ggaggtgctt aagcagaagc attaacttct 1860
ctggaaaggg gggagctggg gaaactcaaa cttttcccct gtcctgatgg tcagctccct 1920
tctctgtagg gaactgtggg gtcccccatc cccatcctcc agcttctggt actctcctag 1980
agacagaagc aggctggagg taaggccttt gagcccacaa agccttatca agtgtcttcc 2040
atcatggatt cattacagct taatcaaaat aacgccccag ataccagccc ctgtatggca 2100
ctggcattgt ccctgtgcct aacaccagcg tttgaggggc tgccttcctg ccctacagag 2160
gtctctgccg gctctttcct tgctcaacca tggctgaagg aaacagtgca acagcactgg 2220
ctctctccag gatccagaag gggtttggtc tggacttcct tgctctcccc tcttctcaag 2280
tgccttaata gtagggtaag ttgttaagag tgggggagag caggctggca gctctccagt 2340
caggaggcat agtttttagt gaacaatcaa agcacttgga ctcttgctct ttctactctg 2400
aactaataaa gctgttgcca agctggacgg cacgagctcg tgcc 2444

<210> 315
<211> 732
<212> DNA
<213> Homo sapiens

<400> 315
tgctgcgaac cacgtgggtc ccgggcgcgt ttcgggtgct ggcggctgca gccggagttc 60
aaacctaagc agctggaagg aaccatggcc aactgtgagc gtaccttcat tgcgatcaaa 120
ccagatgggg tccagcgggg tcttgtggga gagattatca agcgttttga gcagaaagga 180
ttccgccttg ttggtctgaa attcatgcaa gcttccgaag atcttctcaa ggaacactac 240
gttgacctga aggaccgtcc attctttgcc ggcctggtga aatacatgca ctcagggccg 300
gtagttgcca tggtctggga ggggctgaat gtggtgaaga cgggccgagt catgctcggg 360
gagaccaacc ctgcagactc caagcctggg accatccgtg gagacttctg catacaagtt 420
ggcaggaaca ttatacatgg cagtgattct gtggagagtg cagagaagga gatcggcttg 480
tggtttcacc ctgaggaact ggtagattac acgagctgtg ctcagaactg gatctatgaa 540
tgacaggagg gcagaccaca ttgcttttca catccatttc ccctccttcc catgggcaga 600
ggaccaggct gtaggaaatc tagttattta caggaacttc atcataattt ggagggaagc 660
tcttggagct gtgagttctc cctgtacagt gttaccatcc ccgaccatct gattaaaatg 720
cttcctccca gc 732

<210> 316
<211> 2422
<212> DNA
<213> Homo sapiens

<400> 316
gtcagcctcc cttccaccgc catattgggc cactaaaaaa agggggctcg tcttttcggg 60
gtgtttttct ccccctcccc tgtccccgct tgctcacggc tctgcgactc cgacgccggc 120
aaggtttgga gagcggctgg gttcgcggga cccgcgggct tgcacccgcc cagactcgga 180
cgggctttgc caccctctcc gcttgcctgg tcccctctcc tctccgccct cccgctcgcc 240
agtccatttg atcagcggag actcggcggc cgggccgggg cttccccgca gcccctgcgc 300
gctcctagag ctcgggccgt ggctcgtcgg ggtctgtgtc ttttggctcc gagggcagtc 360
gctgggcttc cgagaggggt tcgggccgcg taggggcgct ttgttttgtt cggttttgtt 420
tttttgagag tgcgagagag gcggtcgtgc agacccggga gaaagatgtc aaacgtgcga 480
gtgtctaacg ggagccctag cctggagcgg atggacgcca ggcaggcgga gcaccccaag 540
ccctcggcct gcaggaacct cttcggcccg gtggaccacg aagagttaac ccgggacttg 600
gagaagcact gcagagacat ggaagaggcg agccagcgca agtggaattt cgattttcag 660
aatcacaaac ccctagaggg caagtacgag tggcaagagg tggagaaggg cagcttgccc 720
gagttctact acagaccccc gcggcccccc aaaggtgcct gcaaggtgcc ggcgcaggag 780
agccaggatg tcagcgggag ccgcccggcg gcgcctttaa ttggggctcc ggctaactct 840
gaggacacgc atttggtgga cccaaagact gatccgtcgg acagccagac ggggttagcg 900
gagcaatgcg caggaataag gaagcgacct gcaaccgacg attcttctac tcaaaacaaa 960
agagccaaca gaacagaaga aaatgtttca gacggttccc caaatgccgg ttctgtggag 1020
cagacgccca agaagcctgg cctcagaaga cgtcaaacgt aaacagctcg aattaagaat 1080
atgtttcctt gtttatcaga tacatcactg cttgatgaag caaggaagat atacatgaaa 1140
atttaaaaa tacatatcgc tgacttcatg gaatggacat cctgtataag cactgaaaaa 1200
caacaacaca ataacactaa aattttaggc actcttaaat gatctgcctc taaaagcgtt 1260
ggatgtagca ttatgcaatt aggtttttcc ttatttgctt cattgtacta cctgtgtata 1320
tagtttttac cttttatgta gcacataaac tttggggaag ggagggcagg gtggggctga 1380
ggaactgacg tggagcgggg tatgaagagc ttgctttgat ttacagcaag tagataaata 1440
tttgacttgc atgaagagaa gcaattttgg ggaagggttt gaattgtttt ctttaaagat 1500
gtaatgtccc tttcagagac agctgatact tcatttaaaa aaatcacaaa aatttgaaca 1560
ctggctaaag ataattgcta tttattttta caagaagttt attctcattt gggagatctg 1620
gtgatctccc aagctatcta aagtttgtta gatagctgca tgtggctttt ttaaaaaagc 1680
aacagaaacc tatcctcact gccctcccca gtctctctta aagttggaat ttaccagtta 1740
attactcagc agaatggtga tcactccagg tagtttgggg caaaaatccg aggtgcttgg 1800
gagttttgaa tgttaagaat tgaccatctg cttttattaa atttgttgac aaaatttttct 1860
cattttcttt tcacttcggg ctgtgtaaac acagtcaaaa taattctaaa tccctcgata 1920
tttttaaaga tctgtaagta acttcacatt aaaaaatgaa atattttta atttaaagct 1980
tactctgtcc atttatccac aggaaagtgt tatttttaaa ggaaggttca tgtagagaaa 2040
agcacacttg taggataagt gaaatggata ctacatcttt aaacagtatt tcattgcctg 2100
tgtatggaaa aaccatttga agtgtacctg tgtacataac tctgtaaaaa cactgaaaaa 2160
ttatactaac ttatttatgt taaaagattt tttttaatct agacaatata caagccaaag 2220
tggcatgttt tgtgcatttg taaatgctgt gttgggtaga ataggtttc ccctcttttg 2280
ttaaataata tggctatgct taaaaggttg catactgagc caagtataat tttttgtaat 2340
gtgtgaaaaa gatgccaatt attgttacac attaagtaat caataaagaa aacttccata 2400
gctaaaaaaa aaaaaaaaaa aa 2422

<210> 317
<211> 5061
<212> DNA
<213> Homo sapiens

<400> 317
atggctcaga tatttagcaa cagcggattt aaagaatgtc cattttcaca tccggaacca 60
acaagagcaa aagatgtgga caaagaagaa gcattacaga tggaagcaga ggctttagca 120
aaactgcaaa aggatagaca agtgactgac aatcagagag gctttgagtt gtcaagcagc 180
accagaaaaa aagcacaggt ttataacaag caggattatg atctcatggt gtttcctgaa 240
tcagattccc aaaaaagagc attagatatt gatgtagaaa agctcaccca agctgaactt 300
gagaaactat tgctggatga cagtttcgag actaaaaaaa cacctgtatt accagttact 360
cctattctga gcccttcctt ttcagcacag ctctatttta gacctactat tcagagagga 420
cagtggccac ctggattacc tgggccttcc acttatgctt taccttctat ttatccttct 480
acttacagta aacaggctgc attccaaaat ggcttcaatc caagaatgcc cacttttcca 540
tctacagaac ctatatattt aagtcttccg ggacaatctc catatttctc atatcctttg 600
acacctgcca cacccttca tccacaagga agcttaccta tctatcgtcc agtagtcagt 660
actgacatgg caaaactatt tgacaaaata gctagtacat cagaattttt aaaaaatggg 720
aaagcaagga ctgatttgga gataacagat tcaaaagtca gcaatctaca ggtatctcca 780
aagtctgagg atatcagtaa atttgactgg ttagacttgg atcctctaag taagcctaag 840
gtggataatg tggaggtatt agaccatgag gaagagaaaa atgtttcaag tttgctagca 900
aaggatcctt gggatgctgt tcttcttgaa gagagatcga cagcaaattg tcatcttgaa 960
agaaaggtga atggaaaatc cctttctgtg gcaactgtta caagaagcca gtctttaaat 1020
attcgaacaa ctcagcttgc aaaagcccag ggccatatat ctcagaaaga cccaaatggg 1080
accagtagtt tgccaactgg aagttctctt cttcaagaag ttgaagtaca gaatgaggag 1140

39740-0001PCT.txt

```
atggcagctt tttgtcgatc cattacaaaa ttgaagacca aatttccata taccaatcac 1200
cgcacaaacc caggctattt gttaagtcca gtcacagcgc aaagaaacat atgcggagaa 1260
aatgctagtg tgaaggtctc cattgacatt gaaggatttc agctaccagt tacttttacg 1320
tgtgatgtga gttctactgt agaaatcatt ataatgcaag cccttttgctg ggtacatgat 1380
gacttgaatc aagtagatgt tggcagctat gttctaaaag tttgtggtca agaggaagtg 1440
ctgcagaata atcattgcct tggaagtcat gagcatattc aaaactgtcg aaaatgggac 1500
acagaaatta gactacaact cttgaccttc agtgcaatgt gtcaaaatct ggcccgaaca 1560
gcagaagatg atgaaacacc cgtggattta aacaaacacc tgtatcaaat agaaaaacct 1620
tgcaaagaag ccatgacgag acaccctgtt gaagaactct tagattctta tcacaaccaa 1680
gtagaactgg ctcttcaaat tgaaaaccaa caccgagcag tagatcaagt aattaaagct 1740
gtaagaaaaa tctgtagtgc tttagatggt gtcgagactc ttgccattac agaatcagta 1800
aagaagctaa agagagcagt taatcttcca aggagtaaaa ctgctgatgt gacttctttg 1860
tttggaggag aagacactag caggagttca actaggggct cacttaatcc tgaaaatcct 1920
gttcaagtaa gcataaacca attaactgca gcaatttatg atcttctcag actccatgca 1980
aattctggta ggagtcctac agactgtgcc caaagtagca agagtgtcaa ggaagcatgg 2040
actacaacag agcagctcca gtttactatt tttgctgctc atggaatttc aagtaattgg 2100
gtatcaaatt atgaaaaata ctacttgata tgttcactgt ctcacaatgg aaaggatctt 2160
tttaaaccta ttcaatcaaa gaaggttggc acttacaaga atttcttcta tcttattaaa 2220
tgggatgaac taatcatttt tcctatccag atatcacaat tgccattaga atcagttctt 2280
caccttactc tttttggaat tttaaatcag agcagtggaa gttcccctga ttctaataag 2340
cagagaaagg gaccagaagc tttgggcaaa gtttctttac ctctttgtga ctttagacgg 2400
tttttaacat gtggaactaa acttctatat ctttggactt catcacatac aaattctgtt 2460
cctggaacag ttaccaaaaa aggatatgtc atggaaagaa tagtgctaca ggttgatttt 2520
ccttctcctg catttgatat tatttataca actcctcaag ttgacagaag cattatacag 2580
caacataact tagaaacact agagaatgat ataaaaggga aacttcttga tattcttcat 2640
aaagactcat cacttggact ttctaaagaa gataaagctt ttttatggga gaaacgttat 2700
tattgcttca aacacccaaa ttgtcttcct aaaatattag caagcgcccc aaactggaaa 2760
tggggtaatc ttgccaaaac ttactcattg cttcaccagt ggcctgcatt gtacccacta 2820
attgcattgg aacttcttga ttcaaaattt gctgatcagg aagtaagatc cctagctgtg 2880
acctggattg aggccattag tgatgatgag ctaacagatc ttcttccaca gtttgtacaa 2940
gctttgaaat atgaaattta cttgaatagt tcattagtgc aattcctttt gtccagggca 3000
ttgggaaata tccagatagc acacaattta tattggcttc tcaaagatgc cctgcatgat 3060
gtacagttta gtacccgata cgaacatgtt ttgggtgctc tcctgtcagt aggaggaaaa 3120
cgacttagag aagaacttct aaaacagacg aaacttgtac agcttttagg aggagtagca 3180
gaaaaagtaa ggcaggctag tggatcagcc agacaggttg ttctccaaag aagtatggaa 3240
cgagtacagt cctttttca gaaaaataaa tgccgtctcc ctctcaagcc aagtctagtg 3300
gcaaaagaat taaatattaa gtcgtgttcc ttcttcagtt ctaatgctgt cccccttaaaa 3360
gtcacaatgg tgaatgctga ccctctggga gaagaaatta atgtcatgtt taaggttggt 3420
gaagatcttc ggcaagatat gttagcttta cagatgataa agattatgga taagatctgg 3480
cttaaagaag gactagatct gaggatggta attttcaaat gtctctcaac tggcagagat 3540
cgaggcatgg tggagctggt tcctgcttcc gataccctca ggaaaatcca agtggaatat 3600
ggtgtgacag gatcctttaa agataaacca cttgcagagt ggctaaggaa atacaatccc 3660
tctgaagaag aatatgaaaa ggcttcagag aactttatct attcctgtgc tggatgctgt 3720
gtagccacct atgttttagg catctgtgat cgacacaatg acaatataat gcttcgaagc 3780
acgggacaca tgtttcacat tgactttgga aagtttttgg gacatgcaca gatgtttggc 3840
agcttcaaaa gggatcgggc tccttttgtg ctgacctctg atatggcata tgtcattaat 3900
gggggtgaaa agcccaccat tcgttttcag ttgtttgtgg acctctgctg tcaggcctac 3960
aacttgataa gaaagcagac aaaccttttt cttaacctcc tttcactgat gattccttca 4020
gggttaccag aacttacaag tattcaagat ttgaaatacg ttagagatgc acttcaaccc 4080
caaactacag acgcagaagc tacaattttc tttactaggc ttattgaatc aagtttggga 4140
agcattgcca caaagtttaa cttcttcatt cacaaccttg ctcagcttcg tttttctggt 4200
cttccttcta atgatgagcc catcctttca ttttcaccta aaacatactc ctttagacaa 4260
gatggtcgaa tcaaggaagt ctctgttttt acatatcata agaaatacaa cccagataaa 4320
cattatattt atgtagtccg aattttgtgg gaaggacaga ttgaaccatc atttgtcttc 4380
cgaacatttg tcgaatttca ggaacttcac aataagctca gtattatttt tccactttgg 4440
aagttaccag gctttcctaa taggatggtt ctaggaagaa cacacataaa agatgtagca 4500
gccaaaagga aaattgagtt aaacagttac ttacagagtt tgatgaatgc ttcaacggat 4560
gtagcagagt gtgatcttgt ttgtactttc ttccaccctt tacttcgtga tgagaaagct 4620
gaagggatag ctaggtctgc agatgcaggt tccttcagtc ctactccagg ccaaatagga 4680
ggagctgtga aattatccat ctcttaccga aatggtactc ttttcatcat ggtgatgcat 4740
atcaaagatc ttgttactga agatggagct gacccaaatc catatgtcaa aacatacctta 4800
cttccagata accacaaaac atccaaacgt aaaaccaaaa tttcacgaaa aacgaggaat 4860
ccgacattca atgaaatgct tgtatacagt ggatatagca aagaaaccct aagacagcga 4920
gaacttcaac taagtgtact cagtgcagaa tctctgcggg agaatttttt cttgggtgga 4980
gtaaccctgc ctttgaaaga tttcaacttg agcaaagaga cggttaaatg gtatcagctg 5040
actgcggcaa catacttgta a                                            5061
```

<210> 318
<211> 3014
<212> DNA
<213> Homo sapiens

<400> 318
ctgaccagcg ccgccctccc ccgcccccga cccaggaggt ggagatccct ccggtccagc 60
cacattcaac acccactttc tcctccctct gcccctatat tcccgaaacc ccctcctcct 120
tccctttcc ctcctccctg gagacggggg aggagaaaag gggagtccag tcgtcatgac 180
tgagctgaag gcaaagggtc cccgggctcc ccacgtggcg ggcggcccgc cctcccccga 240
ggtcggatcc ccactgctgt gtcgcccagc cgcaggtccg ttcccgggga gccagacctc 300
ggacaccttg cctgaagttt cggccatacc tatctccctg gacgggctac tcttccctcg 360
gccctgccag ggacaggacc cctccgacga aaagacgcag gaccagcagt cgctgtcgga 420
cgtggagggc gcatattcca gagctgaagc tacaaggggt gctggaggca gcagttctag 480
tcccccagaa aaggacagcg gactgctgga cagtgtcttg gacactctgt tggcgccctc 540
aggtcccggg cagagccaac ccagccctcc cgcctgcgag gtcaccagct cttggtgcct 600
gtttggcccc gaacttcccg aagatccacc ggctgccccc gccacccagc gggtgttgtc 660
cccgctcatg agccggtccg ggtgcaaggt tggagacagc tccgggacgg cagctgccca 720
taaagtgctg ccccggggcc tgtcaccagc ccggcagctg ctgctcccgg cctctgagag 780
ccctcactgg tccgggggccc cagtgaagcc gtctccgcag gccgctgcgg tggaggttga 840
ggaggaggat ggctctgagt ccgaggagtc tgcgggtccg cttctgaagg gcaaacctcg 900
ggctctgggt ggcgcggcgg ctggaggagg agccgcggct gtcccgccgg gggcggcagc 960
aggaggcgtc gccctggtcc ccaaggaaga ttcccgcttc tcagcgccca gggtcgccct 1020
ggtggagcag gacgcgccga tggcgcccgg gcgctccccg ctggccacca cggtgatgga 1080
tttcatccac gtgcctatcc tgcctctcaa tcacgcctta ttggcagccc gcactcggca 1140
gctgctggaa gacgaaagtt acgacggcgg ggccggggct gccagcgcct ttgccccgcc 1200
gcggagttca ccctgtgcct cgtccacccc ggtcgctgta ggcgacttcc ccgactgcgc 1260
gtacccgccc gacgccgagc ccaaggacga cgcgtaccct ctctatagcg acttccagcc 1320
gcccgctcta aagataaagg aggaggagga aggcgcggag gcctccgcgc gctccccgcg 1380
ttcctacctt gtggccggtg ccaaccccgc agccttcccg gatttcccgt tggggccacc 1440
gccccgctg ccgccgcgag cgaccccatc cagacccggg gaagcggcgg tgacggccgc 1500
acccgccagt gcctcagtct cgtctgcgtc ctcctcgggg tcgaccctgg agtgcatcct 1560
gtacaaagcg gagggcgcgc cgccccagca gggcccgttc gcgccgccgc cctgcaaggc 1620
gccgggcgcg agcggctgcc tgctcccgcg ggacggcctg ccctccacct ccgcctctgc 1680
cgccgccgcc ggggcggccc ccgcgctcta ccctgcactc ggcctcaacg ggctcccgca 1740
gctcggctac caggccgccg tgctcaagga gggcctgccg caggtctacc cgccctatct 1800
caactacctg aggccggatt cagaagccag ccagagccca caatacagct tcgagtcatt 1860
acctcagaag atttgtttaa tctgtgggga tgaagcatca ggctgtcatt atggtgtcct 1920
tacctgtggg agctgtaagg tcttctttaa gagggcaatg gaagggcagc acaactactt 1980
atgtgctgga agaaatgact gcatcgttga taaaatccgc agaaaaaact gcccagcatg 2040
tcgccttaga aagtgctgtc aggctggcat ggtccttgga ggtcgaaaat ttaaaaagtt 2100
caataaagtc agagttgtga gagcactgga tgctgttgct ctcccacagc cagtgggcgt 2160
tccaaatgaa agccaagccc taagccagag attcactttt tcaccaggtc aagacataca 2220
gttgattcca ccactgatca acctgttaat gagcattgaa ccagatgtga tctatgcagg 2280
acatgacaac acaaaacctg acacctccag ttctttgctg acaagtctta atcaactagg 2340
cgagaggcaa cttctttcag tagtcaagtg gtctaaatca ttgccaggtt ttcgaaactt 2400
acatattgat gaccagataa ctctcattca gtattcttgg atgagcttaa tggtgtttgg 2460
tctaggatgg agatcctaca aacacgtcag tgggcagatg ctgtattttg cacctgatct 2520
aatactaaat gaacagcgga tgaaagaatc atcattctat tcattatgcc ttaccatgtg 2580
gcagatccca caggagtttg tcaagcttca agttagccaa gaagagttcc tctgtatgaa 2640
agtattgtta cttcttaata caattccttt ggaagggcta cgaagtcaaa cccagtttga 2700
ggagatgagg tcaagctaca ttagagagct catcaaggca attggtttga ggcaaaaagg 2760
agttgtgtcg agctcacagc gtttctatca acttacaaaa cttcttgata acttgcatga 2820
tcttgtcaaa caacttcatc tgtactgctt gaatacattt atccagtccc gggcactgag 2880
tgttgaattt ccagaaatga tgtctgaagt tattgctgca caattaccca agatattggc 2940
agggatggtg aaaccccttc tctttcataa aaagtgaatg tcatcttttt cttttaaaga 3000
attaaatttt gtgg 3014

<210> 319
<211> 2148
<212> DNA
<213> Homo sapiens

<400> 319
gcttcagggt acagctcccc cgcagccaga agccgggcct gcagcgcctc agcaccgctc 60
cgggacaccc cacccgcttc ccaggcgtga cctgtcaaca gcaacttcgc ggtgtggtga 120
actctctgag gaaaaaccat tttgattatt actctcagac gtgcgtggca acaagtgact 180

```
gagacctaga aatccaagcg ttggaggtcc tgaggccagc ctaagtcgct tcaaaatgga 240
acgaaggcgt ttgtggggtt ccattcagag ccgatacatc agcatgagtg tgtggacaag 300
cccacggaga cttgtggagc tggcagggca gagcctgctg aaggatgagg ccctggccat 360
tgccgccctg gagttgctgc ccagggagct cttcccgcca ctcttcatgg cagcctttga 420
cgggagacac agccagaccc tgaaggcaat ggtgcaggcc tggcccttca cctgcctccc 480
tctgggagtg ctgatgaagg gacaacatct tcacctggag accttcaaag ctgtgcttga 540
tggacttgat gtgctccttg cccaggaggt tcgccccagg aggtggaaac ttcaagtgct 600
ggatttacgg aagaactctc atcaggactt ctggactgta tggtctggaa acagggccag 660
tctgtactca tttccagagc cagaagcagc tcagcccatg acaaagaagc gaaaagtaga 720
tggtttgagc acagaggcag agcagccctt cattccagta gaggtgctcg tagacctgtt 780
cctcaaggaa ggtgcctgtg atgaattgtt ctcctacctc attgagaaag tgaagcgaaa 840
gaaaaatgta ctacgcctgt gctgtaagaa gctgaagatt tttgcaatgc ccatgcagga 900
tatcaagatg atcctgaaaa tggtgcagct ggactctatt gaagatttgg aagtgacttg 960
tacctggaag ctacccacct tggcgaaatt ttctccttac ctgggccaga tgattaatct 1020
gcgtagactc ctcctctccc acatccatgc atcttcctac atttccccgg agaaggaaga 1080
gcagtatatc gcccagttca cctctcagtt cctcagtctg cagtgcctgc aggctctcta 1140
tgtggactct ttatttttcc ttagaggccg cctggatcag ttgctcaggc acgtgatgaa 1200
cccccttgga accctctcaa taactaactg ccggctttcg gaaggggatg tgatgcatct 1260
gtcccagagt cccagcgtca gtcagctaag tgtcctgagt ctaagtgggg tcatgctgac 1320
cgatgtaagt cccgagcccc tccaagctct gctggagaga gcctctgcca ccctccagga 1380
cctggtcttt gatgagtgtg ggatcacgga tgatcagctc cttgccctcc tgccttccct 1440
gagccactgc tcccagctta caaccttaag cttctacggg aattccatct ccatatctgc 1500
cttgcagagt ctcctgcagc acctcatcgg gctgagcaat ctgacccacg tgctgtatcc 1560
tgtccccctg gagagttatg aggacatcca tggtaccctc cacctggaga ggcttgccta 1620
tctgcatgcc aggctcaggg agttgctgtg tgagttgggg cggcccagca tggtctggct 1680
tagtgccaac ccctgtcctc actgtgggga cagaaccttc tatgacccgg agcccatcct 1740
gtgcccctgt ttcatgccta actagctggg tgcacatatc aaatgcttca ttctgcatac 1800
ttggacacta aagccaggat gtgcatgcat cttgaagcaa caaagcagcc acagtttcag 1860
acaaatgttc agtgtgagtg aggaaaacat gttcagtgag gaaaaaacat tcagacaaat 1920
gttcagtgag gaaaaaaagg ggaagttggg gataggcaga tgttgacttg aggagttaat 1980
gtgatctttg gggagataca tcttatagag ttagaaatag aatctgaatt tctaaaggga 2040
gattctggct tgggaagtac atgtaggagt taatccctgt gtagactgtt gtaaagaaac 2100
tgttgaaaat aaagagaagc aatgtgaagc aaaaaaaaaa aaaaaaaa              2148
```

<210> 320
<211> 540
<212> DNA
<213> Homo sapiens

<400> 320

```
atccctgact cggggtcgcc tttggagcag agaggaggca atggccacca tggagaacaa 60
ggtgatctgc gccctggtcc tggtgtccat gctggccctc ggcaccctgg ccgaggccca 120
gacagagacg tgtacagtgg ccccccgtga aagacagaat tgtggttttc ctggtgtcac 180
gccctcccag tgtgcaaata agggctgctg tttcgacgac accgttcgtg ggtcccctg 240
gtgcttctat cctaatacca tcgacgtccc tccagaagag gagtgtgaat tttagacact 300
tctgcaggga tctgcctgca tcctgacggg gtgccgtccc cagcacggtg attagtccca 360
gagctcggct gccacctcca ccggacacct cagacacgct tctgcagctg tgcctcggct 420
cacaacacag attgactgct ctgactttga ctactcaaaa ttggcctaaa aattaaaaga 480
gatcgatatt aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540
```

<210> 321
<211> 2346
<212> DNA
<213> Homo sapiens

<400> 321

```
gcacgaggct gcggcgggtc cgggcccatg aggcgacgaa ggaggcggga cggcttttac 60
ccagccccgg acttccgaga cagggaagct gaggacatgg caggagtgtt tgacatagac 120
ctggaccagc cagaggacgc gggctctgag gatgagctgg aggaggggga tcagttaaat 180
gaaagcatgg accatggggg agttggacca tatgaacttg gcatggaaca ttgtgagaaa 240
tttgaaatct cagaaactag tgtgaacaga gggccagaaa aaatcagacc agaatgtttt 300
gagctacttc gggtacttgg taaagggggc tatggaaagg tttttcaagt acgaaaagta 360
acaggagcaa atactgggaa aatatttgcc atgaaggtgc ttaaaaaggc aatgatagta 420
agaaatgcta aagatacagc tcatacaaaa gcagaacgga atattctgga ggaagtaaag 480
catcccttca tcgtggattt aatttatgcc tttcagactg gtggaaaact ctacctcatc 540
cttgagtatc tcagtggagg agaactattt atgcagttag aaagagaggg aatatttatg 600
gaagacactg cctgctttta cttggcagaa atctccatgg ctttggggca tttacatcaa 660
```

```
aaggggatca tctacagaga cctgaagccg gagaatatca tgcttaatca ccaaggtcat 720
gtgaaactaa cagactttgg actatgcaaa gaatctattc atgatggaac agtcacacac 780
acattttgtg gaacaataga atacatggcc cctgaaatct tgatgagaag tggccacaat 840
cgtgctgtgg attggtggag tttgggagca ttaatgtatg acatgctgac tggagcaccc 900
ccattcactg gggagaatag aaagaaaaca attgacaaaa tcctcaaatg taaactcaat 960
ttgcctccct acctcacaca agaagccaga gatctgctta aaaagctgct gaaaagaaat 1020
gctgcttctc gtctgggagc tggtcctggg gacgctggag aagttcaagc tcatccattc 1080
tttagacaca ttaactggga agaacttctg gctcgaaagg tggagccccc ctttaaacct 1140
ctgttgcaat ctgaagagga tgtaagtcag tttgattcca agtttacacg tcagacacct 1200
gtcgacagcc cagatgactc aactctcagt gaaagtgcca atcaggtctt tctgggtttt 1260
acatatgtgg ctccatctgt acttgaaagt gtgaaagaaa agttttcctt tgaaccaaaa 1320
atccgatcac ctcgaagatt tattggcagc ccacgaacac ctgtcagccc agtcaaattt 1380
tctcctgggg atttctgggg aagaggtgct tcggccagca cagcaaatcc tcagacacct 1440
gtggaatacc caatggaaac aagtggcata gagcagatgg atgtgacaat gagtggggaa 1500
gcatcggcac cacttccaat acgacagccg aactctgggc catacaaaaa acaagctttt 1560
cccatgatct ccaaacggcc agagcacctg cgtatgaatc tatgacagag caatgctttt 1620
aatgaattta aggcaaaaag gtggagaggg agatgtgtga gcatcctgca aggtgaaaca 1680
agactcaaaa tgacagtttc agagagtcaa tgtcattaca tagaacactt cggacacagg 1740
aaaaataaac gtggatttta aaaaatcaat caatggtgca aaaaaaaact taaagcaaaa 1800
tagtattgct gaactcttag gcacatcaat taattgattc ctcgcgacat ctttctcaac 1860
cttatcaagg atttcatgt tgatgactcg aaactgacag tattaagggt aggatgttgc 1920
tctgaatcac tgtgagtctg atgtgtgaag aagggtatcc tttcattagg caagtacaaa 1980
ttgcctataa tacttgcaac taaggacaaa ttagcatgca agcttggtca aacttttccc 2040
aggcaaaatg ggaaggcaaa gacaaaagaa acttaccaat tgatgtttta cgtgcaaaca 2100
acctgaatct tttttttata taaatatata tttttcaaat agatttttga ttcagctcat 2160
tatgaaaaac atcccaaact ttaaaatgcg aaattattgg ttggtgtgaa gaaagccaga 2220
caacttctgt ttcttctctt ggtgaaataa taaaatgcaa atgaatcatt gttaacacag 2280
ctgtggctcg tttgagggat tggggtggac ctggggttta ttttcagtaa cccagctgcg 2340
gagcct 2346

<210> 322
<211> 2420
<212> DNA
<213> Homo sapiens

<400> 322
tccggggcgg cccccggcag ccagcgcgac gttccaaaat cgaacctcag tggcggcgct 60
cggaagcgga actctgccgg ggccgcgccg gctacattgt ttcctccccc cgactccctc 120
ccgcccccctt cccccgcctt tcttccctcc gcgacccggg ccgtgcgtcc gtccccctgc 180
ctctgcctgg cggtccctcc tcccctctcc ttgcacccat acctctttgt accgcacccc 240
ctggggaccc ctgcgcccct cccctccccc ctgaccgcat ggaccgtccc gcaggccgct 300
gatgccgccc gcggcgaggt ggcccggacc gcagtgcccc aagagagctc taatggtacc 360
aagtgacagg ttggctttac tgtgactcgg ggacgccaga gctcctgaga agatgtcagc 420
aatacaggcc gcctggccat ccggtacaga atgtattgcc aagtacaact tccacggcac 480
tgccgagcag gacctgccct tctgcaaagg agacgtgctc accattgtgg ccgtcaccaa 540
ggaccccaac tggtacaaag ccaaaaacaa ggtgggccgt gagggcatca tcccagccaa 600
ctacgtccag aagcgggagg gcgtgaaggc gggtaccaaa ctcagcctca tgccttggtt 660
ccacggcaag atcacacggg agcaggctga gcggcttctg tacccgccgg agacaggcct 720
gttcctggtg cgggagagca ccaactaccc cggagactac acgctgtgcg tgagctgcga 780
cggcaaggtg gagcactacc gcatcatgta ccatgccagc aagctcagca tcgacgagga 840
ggtgtacttt gagaacctca tgcagctggt ggagcactac acctcagacg cagatggact 900
ctgtacgcgc ctcattaaac caaaggtcat ggagggcaca gtggcggccc aggatgagtt 960
ctaccgcagc ggctgggccc tgaacatgaa ggagctgaag ctgctgcaga ccatcgggaa 1020
gggggagttc ggagacgtga tgctgggcga ttaccgaggg aacaaagtcg ccgtcaagtg 1080
cattaagaac gacgccactg cccaggcctt cctggctgaa gcctcagtca tgacgcaact 1140
gcggcatagc aacctggtgc agctcctggg cgtgatcgtg gaggagaagg gcgggctcta 1200
catcgtcact gagtacatgg ccaaggggag ccttgtggac tacctgcggt ctaggggtcg 1260
gtcagtgctg ggcggagact gtctcctcaa gttctcgcta gatgtctgcg aggccatgga 1320
atacctggag ggcaacaatt tcgtgcatcg agacctggct gcccgcaatg tgctggtgtc 1380
tgaggacaac gtggccaagg tcagcgactt tggtctcacc aaggaggcgt ccagcaccca 1440
ggacacgggc aagctgccag tcaagtggac agcccctgag gccctgagag agaagaaatt 1500
ctccactaag tctgacgtgt ggagtttcgg aatccttctc tgggaaatct actcctttgg 1560
gcgagtgcct tatccaagaa ttcccctgaa ggacgtcgtc cctcgggtgg agaagggcta 1620
caagatggat gcccccgacg gctgcccgcc cgcagtctat gaagtcatga agaactgctg 1680
gcacctggac gccgccatgc ggccctcctt cctacagctc cgagagcagc ttgagcacat 1740
caaaacccac gagctgcacc tgtgacggct ggcctccgcc tgggtcatgg gcctgtgggg 1800
actgaacctg gaagatcatg gacctggtgc ccctgctcac tgggcccgag cctgaactga 1860
gccccagcgg gctggcgggc ctttttcctg cgtcccagcc tgcacccctc cggccccgtc 1920
```

tctcttggac ccacctgtgg ggcctgggga gcccactgag gggccaggga ggaaggaggc 1980
cacggagcgg gcggcagcgc cccaccacgt cgggcttccc tggcctcccg ccactcgcct 2040
tcttagagtt ttattccttt cctttttgga gatttttttt ccgtgtgttt atttttattt 2100
atttttcaag ataaggagaa agaaagtacc cagcaaatgg gcattttaca agaagtacga 2160
atcttatttt tcctgtcctg cccgtgaggt ggggggggacc gggcccctct ctagggaccc 2220
ctcgccccag cctcattccc cattctgtgt cccatgtccc gtgtctcctc ggtcgccccg 2280
tgtttgcgct tgaccatgtt gcactgtttg catgcgcccg aggcagacgt ctgtcagggg 2340
cttggatttc gtgtgccgct gccacccgcc cacccgcctt gtgagatgga atcgtaataa 2400
accacgccat gaggaaaaaa 2420

<210> 323
<211> 2253
<212> DNA
<213> Homo sapiens

<400> 323
ggaagacttg ggtccttggg tcgcaggtgg gagccgacgg gtgggtagac cgtgggggat 60
atctcagtgg cggacgagga cggcggggac aaggggcggc tggtcggagt ggcggagcgt 120
caagtcccct gtcggttcct ccgtccctga gtgtccttgg cgctgccttg tgcccgccca 180
gcgcctttgc atccgctcct gggcaccgag gcgccctgta ggatactgct tgttacttat 240
tacagctaga ggcatcatgg accgatctaa agaaaactgc atttcaggac ctgttaaggc 300
tacagctcca gttggaggtc caaaacgtgt tctcgtgact cagcaaattc cttgtcagaa 360
tccattacct gtaaatagtg gccaggctca gcgggtcttg tgtccttcaa attcttccca 420
gcgcgttcct ttgcaagcac aaaagcttgt ctccagtcac aagccggttc agaatcagaa 480
gcagaagcaa ttgcaggcaa ccagtgtacc tcatcctgtc tccaggccac tgaataacac 540
ccaaaagagc aagcagcccc tgccatcggc acctgaaaat aatcctgagg aggaactggc 600
atcaaaacag aaaaatgaag aatcaaaaaa gaggcagtgg gctttggaag actttgaaat 660
tggtcgccct ctgggtaaag gaaagtttgg taatgtttat ttggcaagag aaaagcaaag 720
caagtttatt ctggctctta aagtgttatt taaagctcag ctggagaaag ccggagtgga 780
gcatcagctc agaagagaag tagaaataca gtcccacctt cggcatccta atattcttag 840
actgtatggt tatttccatg atgctaccag agtctaccta attctggaat atgcaccact 900
tggaacagtt tatagagaac ttcagaaact ttcaaagttt gatgagcaga gaactgctac 960
ttatataaca gaattggcaa atgccctgtc ttactgtcat tcgaagagag ttattcatag 1020
agacattaag ccagagaact tacttcttgg atcagctgga gagcttaaaa ttgcagattt 1080
tgggtggtca gtacatgctc catcttccag gaggaccact ctctgtggca ccctggacta 1140
cctgccccct gaaatgattg aaggtcggat gcatgatgag aaggtggatc tctggagcct 1200
tggagttctt tgctatgaat ttttagttgg gaagcctcct tttgaggcaa acacatacca 1260
agagacctac aaaagaatat cacgggttga attcacattc cctgactttg taacagaggg 1320
agccagggac ctcatttcaa gactgttgaa gcataatccc agccagaggc caatgctcag 1380
agaagtactt gaacacccct ggatcacagc aaattcatca aaaccatcaa attgccaaaa 1440
caaagaatca gctagcaaac agtcttagga atcgtgcagg gggagaaatc cttgagccag 1500
ggctgccata taacctgaca ggaacatgct actgaagttt attttaccat tgactgctgc 1560
cctcaatcta gaacgctaca caagaaatat ttgttttact cagcaggtgt gccttaacct 1620
ccctattcag aaagctccac atcaataaac atgacactct gaagtgaaag tagccacgag 1680
aattgtgcta cttatactgg ttcataatct ggaggcaagg ttcgactgca gccgccccgt 1740
cagcctgtgc taggcatggt gtcttcacag gaggcaaatc cagagcctgg ctgtggggaa 1800
agtgaccact ctgccctgac cccgatcagt taaggagctg tgcaataacc ttcctagtac 1860
ctgagtgagt gtgtaactta ttgggttggc gaagcctggt aaagctgttg gaatgagtat 1920
gtgattcttt ttaagtatga aaataaagat atatgtacag acttgtattt tttctctggt 1980
ggcattcctt taggaatgct gtgtgtctgt ccggcacccc ggtaggcctg attgggtttc 2040
tagtcctcct taaccactta tctcccatat gagagtgtga aaaataggaa cacgtgctct 2100
acctccattt agggatttgc ttgggataca gaagaggcca tgtgtctcag agctgttaag 2160
ggcttatttt tttaaaacat tggagtcata gcatgtgtgt aaactttaaa tatgcaaata 2220
aataagtatc tatgtctaaa aaaaaaaaaa aaa 2253

<210> 324
<211> 1619
<212> DNA
<213> Homo sapiens

<400> 324
ccgccagatt tgaatcgcgg gacccgttgg cagaggtggc ggcggcggca tgggtgcccc 60
gacgttgccc cctgcctggc agccctttct caaggaccac cgcatctcta cattcaagaa 120
ctggcccttc ttggagggct gcgcctgcac cccggagcgg atggccgagg ctggcttcat 180
ccactgcccc actgagaacg agccagactt ggcccagtgt ttcttctgct tcaaggagct 240
ggaaggctgg gagccagatg acgaccccat agaggaacat aaaaagcatt cgtccggttg 300
cgctttcctt tctgtcaaga agcagtttga agaattaacc cttggtgaat tttgaaact 360
ggacagagaa agagccaaga acaaaattgc aaaggaaacc aacaataaga agaaagaatt 420

```
tgaggaaact gcgaagaaag tgcgccgtgc catcgagcag ctggctgcca tggattgagg 480
cctctggccg gagctgcctg gtcccagagt ggctgcacca cttccagggt ttattccctg 540
gtgccaccag ccttcctgtg ggccccttag caatgtctta ggaaaggaga tcaacatttt 600
caaattagat gtttcaactg tgctcctgtt ttgtcttgaa agtggcacca gaggtgcttc 660
tgcctgtgca gcgggtgctg ctggtaacag tggctgcttc tctctctctc tctctttttt 720
gggggctcat ttttgctgtt ttgattcccg ggcttaccag gtgagaagtg agggaggaag 780
aaggcagtgt ccctttgct agagctgaca gctttgttcg cgtgggcaga gccttccaca 840
gtgaatgtgt ctggacctca tgttgttgag gctgtcacag tcctgagtgt ggacttggca 900
ggtgcctgtt gaatctgagc tgcaggttcc ttatctgtca cacctgtgcc tcctcagagg 960
acagtttttt tgttgttgtg ttttttttgtt ttttttttt ggtagatgca tgacttgtgt 1020
gtgatgagag aatggagaca gagtccctgg ctcctctact gtttaacaac atggctttct 1080
tatttgttt gaattgttaa ttcacagaat agcacaaact acaattaaaa ctaagcacaa 1140
agccattcta agtcattggg gaaacggggt gaacttcagg tggatgagga gacagaatag 1200
agtgatagga agcgtctggc agatactcct tttgccactg ctgtgtgatt agacaggccc 1260
agtgagccgc ggggcacatg ctggccgctc ctccctcaga aaaaggcagt ggcctaaatc 1320
ctttttaaat gacttggctc gatgctgtgg gggactggct gggctgctgc aggccgtgtg 1380
tctgtcagcc caaccttcac atctgtcacg ttctccacac gggggagaga cgcagtccgc 1440
ccaggtcccc gctttctttg gaggcagcag ctcccgcagg gctgaagtct ggcgtaagat 1500
gatggatttg attcgccctc ctccctgtca tagagctgca gggtggattg ttacagcttc 1560
gctggaaacc tctggaggtc atctcggctg ttcctgagaa ataaaaagcc tgtcatttc 1619
```

<210> 325
<211> 5010
<212> DNA
<213> Homo sapiens

<400> 325

```
ggcggctcgg gacggaggac gcgctagtgt gagtgcgggc ttctagaact acaccgaccc 60
tcgtgtcctc ccttcatcct gcggggctgg ctggagcggc cgctccggtg ctgtccagca 120
gccataggga gccgcacggg gagcgggaaa gcggtcgcgg ccccaggcgg ggcggccggg 180
atggagcggg gccgcgagcc tgtggggaag gggctgtggc ggcgcctcga gcggctgcag 240
gttcttctgt gtggcagttc agaatgatgg atcaagctag atcagcattc tctaacttgt 300
ttggtggaga accattgtca tatacccggt tcagcctggc tcggcaagta gatggcgata 360
acagtcatgt ggagatgaaa cttgctgtag atgaagaaga aaatgctgac aataacacaa 420
aggccaatgt cacaaaacca aaaaggtgta gtggaagtat ctgctatggg actattgctg 480
tgatcgtctt tttcttgatt ggatttatga ttggctactt gggctattgt aaaggggtag 540
aaccaaaaac tgagtgtgag agactggcag gaaccgagtc tccagtgagg gaggagccag 600
gagaggactt ccctgcagca cgtcgcttat attgggatga cctgaagaga aagttgtcgg 660
agaaactgga cagcacagac ttcaccagca ccatcaagct gctgaatgaa aattcatatg 720
tccctcgtga ggctggatct caaaaagatg aaaatcttgc gttgtatgtt gaaaatcaat 780
ttcgtgaatt taaactcagc aaagtctggc gtgatcaaca ttttgttaag attcaggtca 840
aagacagcgc tcaaaactcg gtgatcatag ttgataagaa cggtagactt gtttacctgg 900
tggagaatcc tgggggttat gtggcgtata gtaaggctgc aacagttact ggtaaactgg 960
tccatgctaa ttttggtact aaaaaagatt ttgaggattt atacactcct gtgaatggat 1020
ctatagtgat tgtcagagca gggaaaatca cctttgcaga aaaggttgca aatgctgaaa 1080
gcttaaatgc aattggtgtg ttgatataca tggaccagac taaatttccc attgttaacg 1140
cagaactttc attctttgga catgctcatc tggggacagg tgacccttac acacctggat 1200
tcccttcctt caatcacact cagtttccac catctcggtc atcaggattg cctaatatac 1260
ctgtccagac aatctccaga gctgctgcag aaaagctgtt tgggaatatg gaaggagact 1320
gtccctctga ctggaaaaca gactctacat gtaggatggt aacctcagaa agcaagaatg 1380
tgaagctcac tgtgagcaat gtgctgaaag agataaaaat tcttaacatc tttggagtta 1440
ttaaaggctt tgtagaacca gatcactatg ttgtagttgg ggcccagaga gatgcatggg 1500
gccctggagc tgcaaaatcc ggtgtaggca cagctctcct attgaaactt gcccagatgt 1560
tctcagatat ggtcttaaaa gatgggtttc agcccagcag aagcattatc tttgccagtt 1620
ggagtgctgg agactttgga tcggttggtg ccactgaatg gctagaggga tacctttcgt 1680
ccctgcattt aaaggctttc acttatatta atctggataa agcggttctt ggtaccagca 1740
acttcaaggt ttctgccagc ccactgttgt atacgcttat tgagaaaaca atgcaaaatg 1800
tgaagcatcc ggttactggg caatttctat atcaggacag caactgggcc agcaaagttg 1860
agaaactcac tttagacaat gctgctttcc ctttccttgc atattctgga atcccagcag 1920
tttctttctg tttttgcgag gacacagatt atccttattt gggtaccacc atggacacct 1980
ataaggaact gattgagagg attcctgagt tgaacaaagt ggcacgagca gctgcagagg 2040
tcgctggtca gttcgtgatt aaactaaccc atgatgttga attgaacctg gactatgaga 2100
ggtacaacag ccaactgctt tcatttgtga gggatctgaa ccaatacaga gcagacataa 2160
aggaaatggg cctgagttta cagtggctgt attctgctcg tggagacttc ttccgtgcta 2220
cttccagact aacaacagat ttcgggaatg ctgagaaaac agacagattt gtcatgaaga 2280
aactcaatga tcgtgtcatg agagtggagt atcacttcct ctctccctac gtatctccaa 2340
aagagtctcc tttccgacat gtcttctggg gctccggctc tcacacgctg ccagctttac 2400
tggagaactt gaaactgcgt aaacaaaata acggtgcttt taatgaaacg ctgttcagaa 2460
```

accagttggc tctagctact tggactattc agggagctgc aaatgccctc tctggtgacg 2520
tttgggacat tgacaatgag ttttaaatgt gatacccata gcttccatga gaacagcagg 2580
gtagtctggt ttctagactt gtgctgatcg tgctaaattt tcagtagggc tacaaaacct 2640
gatgttaaaa ttccatccca tcatcttggt actactagat gtctttaggc agcagctttt 2700
aatacagggt agataacctg tacttcaagt taaagtgaat aaccacttaa aaaatgtcca 2760
tgatggaata ttcccctatc tctagaattt taagtgcttt gtaatgggaa ctgcctcttt 2820
cctgttgttg ttaatgaaaa tgtcagaaac cagttatgtg aatgatctct ctgaatccta 2880
agggctggtc tctgctgaag gttgtaagtg gttcgcttac tttgagtgat cctccaactt 2940
catttgatgc taaataggag ataccaggtt gaaagacctc tccaaatgag atctaagcct 3000
ttccataagg aatgtagcag gtttcctcat tcctgaaaga aacagttaac tttcagaaga 3060
gatgggcttg ttttcttgcc aatgaggtct gaaatggagg tccttctgct ggataaaatg 3120
aggttcaact gttgattgca ggaataaggc cttaatatgt taacctcagt gtcatttatg 3180
aaaagagggg accagaagcc aaagacttag tatattttct tttcctctgt cccttccccc 3240
ataagcctcc atttagttct ttgttatttt tgtttcttcc aaagcacatt gaaagagaac 3300
cagtttcagg tgtttagttg cagactcagt ttgtcagact ttaaagaata atatgctgcc 3360
aaattttggc caaagtgtta atcttagggg agagctttct gtccttttgg cactgagata 3420
tttattgttt atttatcagt gacagagttc actataaatg gtgttttttt aatagaatat 3480
aattatcgga agcagtgcct tccataatta tgacagttat actgtcggtt tttttaaat 3540
aaaagcagca tctgctaata aaacccaaca gatactggaa gttttgcatt tatggtcaac 3600
acttaagggt tttagaaaac agccgtcagc caaatgtaat tgaataaagt tgaagctaag 3660
atttagagat gaattaaatt taattagggg ttgctaagaa gcgagcactg accagataag 3720
aatgctggtt ttcctaaatg cagtgaattg tgaccaagtt ataaatcaat gtcacttaaa 3780
ggctgtggta gtactcctgc aaaattttat agctcagttt atccaaggtg taactctaat 3840
tcccatttgc aaaatttcca gtacctttgt cacaatccta acacattatc gggagcagtg 3900
tcttccataa tgtataaaga acaaggtagt ttttacctac cacagtgtct gtatcggaga 3960
cagtgatctc catatgttac actaagggtg taagtaatta tcgggaacag tgtttcccat 4020
aatttcttc atgcaatgac atcttcaaag cttgaagatc gttagtatct aacatgtatc 4080
ccaactccta taattcccta tcttttagtt ttagttgcag aaacattttg tggtcattaa 4140
gcattgggtg ggtaaattca accactgtaa aatgaaatta ctacaaaatt tgaaatttag 4200
cttgggtttt tgttaccttt atggtttctc caggtcctct acttaatgag atagcagcat 4260
acatttataa tgtttgctat tgacaagtca ttttaattta tcacattatt tgcatgttac 4320
ctcctataaa cttagtgcgg acaagtttta atccagaatt gaccttttga cttaaagcag 4380
agggactttg tatagaaggt ttgggggctg tggggaagga gagtcccctg aaggtctgac 4440
acgtctgcct acccattcgt ggtgatcaat taaatgtagg tatgaataag ttcgaagctc 4500
cgtgagtgaa ccatcatata aacgtgtagt acagctgttt gtcatagggc agttggaaac 4560
ggcctcctag ggaaaagttc atagggtctc ttcaggttct tagtgtcact tacctagatt 4620
tacagcctca cttgaatgtg tcactactca cagtctcttt aatcttcagt tttatcttta 4680
atctcctctt ttatcttgga ctgacattta gcgtagctaa gtgaaaaggt catagctgag 4740
attcctggtt cgggtgttac gcacacgtac ttaaatgaaa gcatgtggca tgttcatcgt 4800
ataacacaat atgaatacag ggcatgcatt ttgcagcagt gagtctcttc agaaaaccct 4860
tttctacagt tagggttgag ttacttccta tcaagccagt acgtgctaac aggctcaata 4920
ttcctgaatg aaatatcaga ctagtgacaa gctcctggtc ttgagatgtc ttctcgttaa 4980
ggagtagggc cttttggagg taaaggtata 5010

<210> 326
<211> 2574
<212> DNA
<213> Homo sapiens

<400> 326
cctgtttaga cacatggaca acaatcccag cgctacaagg cacacagtcc gcttcttcgt 60
cctcagggtt gccagcgctt cctggaagtc ctgaagctct cgcagtgcag tgagttcatg 120
caccttcttg ccaagcctca gtctttggga tctggggagg ccgcctggtt ttcctccctc 180
cttctgcacg tctgctgggg tctcttcctc tccaggcctt gccgtccccc tggcctctct 240
tcccagctca cacatgaaga tgcacttgca aagggctctg gtggtcctgg ccctgctgaa 300
ctttgccacg gtcagcctct ctctgtccac ttgcaccacc ttggacttcg gccacatcaa 360
gaagaagagg gtggaagcca ttaggggaca gatcttgagc aagctcaggc tcaccagccc 420
ccctgagcca acggtgatga cccacgtccc ctatcaggtc ctggcccttt acaacagcac 480
ccgggagctg ctggaggaga tgcatgggga gagggaggaa ggctgcaccc aggaaaacac 540
cgagtcggaa tactatgcca aagaaatcca taaattcgac atgatccagg ggctggcgga 600
gcacaacgaa ctggctgtct gccctaaagg aattacctcc aaggttttcc gcttcaatgt 660
gtcctcagtg gagaaaaata gaaccaacct attccgagca gaattccggg tcttgcgggt 720
gcccaacccc agctctaagc ggaatgagca gaggatcgag ctcttccaga tccttcggcc 780
agatgagcac attgccaaac agcgctatat cggtggcaag aatctgccca cacggggcac 840
tgccgagtgg ctgtcctttg atgtcactga cactgtgcgt gagtggctgt tgagaagaga 900
gtccaactta ggtctagaaa tcagcattca ctgtccatgt cacacctttc agcccaatgg 960

agatatcctg gaaaacattc acgaggtgat ggaaatcaaa ttcaaaggcg tggacaatga 1020
ggatgaccat ggccgtggag atctggggcg cctcaagaag cagaaggatc accacaaccc 1080
tcatctaatc ctcatgatga ttcccccaca ccggctcgac aacccgggcc agggggtca 1140
gaggaagaag cgggctttgg acaccaatta ctgcttccgc aacttggagg agaactgctg 1200
tgtgcgcccc ctctacattg acttccgaca ggatctgggc tggaagtggg tccatgaacc 1260
taagggctac tatgccaact tctgctcagg cccttgccca tacctccgca gtgcagacac 1320
aacccacagc acggtgctgg gactgtacaa cactctgaac cctgaagcat ctgcctcgcc 1380
ttgctgcgtg ccccaggacc tggagcccct gaccatcctg tactatgttg ggaggacccc 1440
caaagtggag cagctctcca acatggtggt gaagtcttgt aaatgtagct gagaccccac 1500
gtgcgacaga gagaggggag agagaaccac cactgcctga ctgcccgctc ctcgggaaac 1560
acacaagcaa caaacctcac tgagaggcct ggagcccaca accttcggct ccgggcaaat 1620
ggctgagatg gaggtttcct tttggaacat ttctttcttg ctggctctga gaatcacggt 1680
ggtaaagaaa gtgtgggttt ggttagagga aggctgaact cttcagaaca cacagacttt 1740
ctgtgacgca gacagagggg atggggatag aggaaaggga tggtaagttg agatgttgtg 1800
tggcaatggg atttgggcta ccctaaaggg agaaggaagg gcagagaatg gctgggtcag 1860
ggccagactg gaagacactt cagatctgag gttggatttg ctcattgctg taccacatct 1920
gctctaggga atctggatta tgttatacaa ggcaagcatt ttttttttta aagacaggtt 1980
acgaagacaa agtcccagaa ttgtatctca tactgtctgg gattaagggc aaatctatta 2040
cttttgcaaa ctgtcctcta catcaattaa catcgtgggt cactacaggg agaaaatcca 2100
ggtcatgcag ttcctggccc atcaactgta ttgggccttt tggatatgct gaacgcagaa 2160
gaaagggtgg aaatcaaccc tctcctgtct gccctctggg tccctcctct cacctctccc 2220
tcgatcatat ttccccttgg acacttggtt agacgccttc caggtcagga tgcacatttc 2280
tggattgtgg ttccatgcag ccttggggca ttatgggtct tcccccactt cccctccaag 2340
accctgtgtt catttggtgt tcctggaagc aggtgctaca acatgtgagg cattcgggga 2400
agctgcacat gtgccacaca gtgacttggc cccagacgca tagactgagg tataaagaca 2460
agtatgaata ttactctcaa aatctttgta taaataaata tttttggggc atcctggatg 2520
atttcatctt ctggaatatt gtttctagaa cagtaaaagc cttattctaa ggtg 2574

<210> 327
<211> 1421
<212> DNA
<213> Homo sapiens

<400> 327
acttactgcg ggacggcctt ggagagtact cgggttcgtg aacttcccgg aggcgcaatg 60
agctgcatta acctgcccac tgtgctgccc ggctccccca gcaagacccg ggggcagatc 120
caggtgattc tcgggccgat gttctcagga aaaagcacag agttgatgag acgcgtccgt 180
cgcttccaga ttgctcagta caagtgcctg gtgatcaagt atgccaaaga cactcgctac 240
agcagcagct tctgcacaca tgaccggaac accatggagg cgctgcccgc ctgcctgctc 300
cgagacgtgg cccaggaggc cctgggcgtg gctgtcatag gcatcgacga ggggcagttt 360
ttccctgaca tcatggagtt ctgcgaggcc atggccaacg ccgggaagac cgtaattgtg 420
gctgcactgg atgggacctt ccagaggaag ccatttgggg ccatcctgaa cctggtgccg 480
ctggccgaga gcgtggtgaa gctgacggcg gtgtgcatgg agtgcttccg ggaagccgcc 540
tataccaaga ggctcggcac agagaaggag gtcgaggtga ttgggggagc agacaagtac 600
cactccgtgt gtcggctctg ctacttcaag aaggcctcag gccagcctgc cgggccggac 660
aacaaagaga actgcccagt gccaggaaag ccaggggaag ccgtggctgc caggaagctc 720
tttgccccac agcagattct gcaatgcagc cctgccaact gagggacctg caagggccgc 780
ccgctccctt cctgccactg ccgcctactg gacgctgccc tgcatgctgc ccagccactc 840
caggaggaag tcgggaggcg tggagggtga ccacaccttg gccttctggg aactctcctt 900
tgtgtggctg ccccacctgc cgcatgctcc ctcctctcct acccactggt ctgcttaaag 960
cttccctctc agctgctggg acgatcgccc aggctggagc tggccccgct tggtggcctg 1020
ggatctggca cactccctct ccttggggtg agggacagag ccccacgctg ttgacatcag 1080
cctgcttctt cccctctgcg gctttcactg ctgagtttct gttctccctg ggaagcctgt 1140
gccagcacct ttgagccttg gcccacactg aggcttaggc ctctctgcct gggatgggct 1200
cccaccctcc cctgaggatg gcctggattc acgccctctt gtttcctttt gggctcaaag 1260
cccttcctac ctctggtgat ggtttccaca ggaacaacag catctttcac caagatgggt 1320
ggcaccaacc ttgctgggac ttggatccca ggggcttatc tcttcaagtg tggagagggc 1380
agggtccacg cctctgctgt agcttatgaa attaactaat t 1421

<210> 328
<211> 4604
<212> DNA
<213> Homo sapiens

<400> 328
ggaacagctt gtccacccgc cggccggacc agaagccttt gggtctgaag tgtctgtgag 60
acctcacaga agagcacccc tgggctccac ttacctgccc cctgctcctt cagggatgga 120
ggcaatggcg gccagcactt ccctgcctga ccctggagac tttgaccgga acgtgccccg 180

gatctgtggg gtgtgtggag accgagccac tggctttcac ttcaatgcta tgacctgtga 240
aggctgcaaa ggcttcttca ggcgaagcat gaagcggaag gcactattca cctgcccctt 300
caacggggac tgccgcatca ccaaggacaa ccgacgccac tgccaggcct gccggctcaa 360
acgctgtgtg gacatcggca tgatgaagga gttcattctg acagatgagg aagtgcagag 420
gaagcgggag atgatcctga agcggaagga ggaggaggcc ttgaaggaca gtctgcggcc 480
caagctgtct gaggagcagc agcgcatcat tgccatactg ctggacgccc accataagac 540
ctacgacccc acctactccg acttctgcca gttccggcct ccagttcgtg tgaatgatgg 600
tggagggagc catccttcca ggcccaactc cagacacact cccagcttct ctggggactc 660
ctcctcctcc tgctcagatc actgtatcac ctcttcagac atgatggact cgtccagctt 720
ctccaatctg gatctgagtg aagaagattc agatgaccct tctgtgaccc tagagctgtc 780
ccagctctcc atgctgcccc acctggctga cctggtcagt tacagcatcc aaaaggtcat 840
tggctttgct aagatgatac caggattcag agacctcacc tctgaggacc agatcgtact 900
gctgaagtca agtgccattg aggtcatcat gttgcgctcc aatgagtcct tcaccatgga 960
cgacatgtcc tggacctgtg gcaaccaaga ctacaagtac cgcgtcagtg acgtgaccaa 1020
agccggacac agcctggagc tgattgagcc cctcatcaag ttccaggtgg gactgaagaa 1080
gctgaacttg catgaggagg agcatgtcct gctcatggcc atctgcatcg tctccccaga 1140
tcgtcctggg gtgcaggacg ccgcgctgat tgaggccatc caggaccgcc tgtccaacac 1200
actgcagacg tacatccgct gccgccaccc gcccccgggc agccacctgc tctatgccaa 1260
gatgatccag aagctagccg acctgcgcag cctcaatgag gagcactcca agcagtaccg 1320
ctgcctctcc ttccagcctg agtgcagcat gaagctaacg ccccttgtgc tcgaagtgtt 1380
tggcaatgag atctcctgac taggacagcc tgtgcggtgc ctgggtgggg ctgctcctcc 1440
agggccacgt gccaggcccg gggctggcgg ctactcagca gccctcctca cccgtctggg 1500
gttcagcccc tcctctgcca cctcccctat ccacccagcc cattctctct cctgtccaac 1560
ctaacccctt tcctgcgggc ttttccccgg tcccttgaga cctcagccat gaggagttgc 1620
tgtttgtttg acaaagaaac ccaagtgggg gcagagggca gaggctggag gcaggccttg 1680
cccagagatg cctccaccgc tgcctaagtg gctgctgact gatgttgagg gaacagacag 1740
gagaaatgca tccattcctc agggacagag acacctgcac ctcccccac tgcaggcccc 1800
gcttgtccag cgcctagtgg ggtctccctc tcctgcctta ctcacgataa ataatcggcc 1860
cacagctccc accccacccc cttcagtgcc caccaacatc ccattgccct ggttatattc 1920
tcacgggcag tagctgtggt gaggtgggtt ttcttcccat cactggagca ccaggcacga 1980
acccacctgc tgagagaccc aaggaggaaa aacagacaaa aacagcctca cagaagaata 2040
tgacagctgt ccctgtcacc aagctcacag ttcctcgccc tgggtctaag ggttggttg 2100
aggtggaagc cctccttcca cggatccatg tagcaggact gaattgtccc cagtttgcag 2160
aaaagcacct gccgacctcg tcctcccct gccagtgcct tacctcctgc ccaggagagc 2220
cagccctccc tgtcctcctc ggatcaccga gagtagccga gagcctgctc ccccaccccc 2280
tccccagggg agagggtctg gagaagcagt gagccgcatc ttctccatct ggcagggtgg 2340
gatggaggag aagaattttc agaccccagc ggctgagtca tgatctccct gccgcctcaa 2400
tgtggttgca aggccgctgt tcaccacagg gctaagagct aggctgccgc accccagagt 2460
gtgggaaggg agagcggggc agtctcgggt ggctagtcag agagagtgtt tgggggttcc 2520
gtgatgtagg gtaaggtgcc ttcttattct cactccacca cccaaaagtc aaaaggtgcc 2580
tgtgaggcag ggcggagtg atacaacttc aagtgcatgc tctctgcagg tcgagcccag 2640
cccagctggt gggaagcgtc tgtccgttta ctccaaggtg ggtctttgtg agagtgagct 2700
gtaggtgtgc gggaccggta cagaaaggcg ttcttcgagg tggatcacag aggcttcttc 2760
agatcaatgc ttgagtttgg aatcggccgc attccctgag tcaccaggaa tgttaaagtc 2820
agtgggaacg tgactgcccc aactcctgga agctgtgtcc ttgcacctgc atccgtagtt 2880
ccctgaaaac ccagagagga atcagacttc acactgcaag agccttggtg tccacctggc 2940
cccatgtctc tcagaattct tcaggtggaa aaacatctga aagccacgtt ccttactgca 3000
gaatagcata tatatcgctt aatcttaaat ttattagata tgagttgttt tcagactcag 3060
actccatttg tattatagtc taatatacag ggtagcaggt accactgatt tggagatatt 3120
tatgggggga gaacttacat tgtgaaactt ctgtacatta attattattg ctgttgttat 3180
tttacaaggg tctagggaga gacccttgtt tgattttagc tgcagaactg tattggtcca 3240
gcttgctctt cagtgggaga aaaacacttg taagttgcta aacgagtcaa tcccctcatt 3300
caggaaaact gacagaggag ggcgtgactc acccaagcca tatataacta gctagaagtg 3360
ggccaggaca ggccgggcgc ggtggctcac gcctgtaatc ccagcagttt gggaggtcga 3420
ggtaggtgga tcacctgagg tcgggagttc gagaccaacc tgaccaacat ggagaaaccc 3480
tgtctctatt aaaaatacaa aaaaaaaaaa aaaaaaaaat agccgggcat ggtggcgcaa 3540
gcctgtaatc ccagctactc aggaggctga ggcagaagaa ttgaacccag gaggtggagg 3600
ttgcagtgag ctgagatcgt gccgttactc tccaacctgg acaacaagag cgaaactccg 3660
tcttagaagt ggaccaggac aggaccagat tttggagtca tggtccggtg tccttttcac 3720
tacaccatgt ttgagctcag acccccactc tcattcccca ggtggctgac ccagtccctg 3780
ggggaagccc tggatttcag aaagagccaa gtctggatct gggacccttt ccttccttcc 3840
ctggcttgta actccaccaa gcccatcaga aggagaagga aggagactca cctctgcctc 3900
aatgtgaatc agaccctacc ccaccacgat gtgccctggc tgctgggctc tccacctcag 3960
gccttggata atgctgttgc ctcatctata acatgcattt gtctttgtaa tgtcaccacc 4020
ttcccagctc tccctctggc cctgcttctt cggggaactc ctgaaatatc agttactcag 4080
ccctgggccc caccacctag gccactcctc caaaggaagt ctaggagctg ggaggaaaag 4140
aaaagagggg aaaatgagtt tttatggggc tgaacgggga gaaaaggtca tcatcgattc 4200
tactttagaa tgagagtgtg aaatagacat ttgtaaatgt aaaactttta aggtatatca 4260

ttataactga aggagaaggt gccccaaaat gcaagatttt ccacaagatt cccagagaca 4320
ggaaaatcct ctggctggct aactggaagc atgtaggaga atccaagcga ggtcaacaga 4380
gaaggcagga atgtgtggca gatttagtga aagctagaga tatggcagcg aaaggatgta 4440
aacagtgcct gctgaatgat ttccaaagag aaaaaaagtt tgccagaagt ttgtcaagtc 4500
aaccaatgta gaaagctttg cttatggtaa taaaaatggc tcatacttat atagcactta 4560
ctttgtttgc aagtactgct gtaaataaat gctttatgca aacc 4604

<210> 329
<211> 2076
<212> DNA
<213> Homo sapiens

<400> 329
cggggaaggg gagggaggag ggggacgagg gctctggcgg gtttggaggg gctgaacatc 60
gcggggtgtt ctggtgtccc ccgccccgcc tctccaaaaa gctacaccga cgcggaccgc 120
ggcggcgtcc tccctcgccc tcgcttcacc tcgcgggctc cgaatgcggg gagctcggat 180
gtccggtttc ctgtgaggct tttacctgac acccgccgcc tttccccggc actggctggg 240
agggcgccct gcaaagttgg gaacgcggag ccccggaccc gctcccgccg cctccggctc 300
gcccaggggg ggtcgccggg aggagcccgg gggagaggga ccaggagggg cccgcggcct 360
cgcaggggcg cccgcgcccc cacccctgcc cccgccagcg gaccggtccc ccaccccccgg 420
tccttccacc atgcacttgc tgggcttctt ctctgtggcg tgttctctgc tcgccgctgc 480
gctgctcccg ggtcctcgcg aggcgcccgc cgccgccgcc gccttcgagt ccggactcga 540
cctctcggac gcggagcccg acgcgggcga ggccacggct tatgcaagca aagatctgga 600
ggagcagtta cggtctgtgt ccagtgtaga tgaactcatg actgtactct acccagaata 660
ttggaaaatg tacaagtgtc agctaaggaa aggaggctgg caacataaca gagaacaggc 720
caacctcaac tcaaggacag aagagactat aaaatttgct gcagcacatt ataatacaga 780
gatcttgaaa agtattgata atgagtggag aaagactcaa tgcatgccac gggaggtgtg 840
tatagatgtg gggaaggagt ttggagtcgc gacaaacacc ttctttaaac ctccatgtgt 900
gtccgtctac agatgtgggg gttgctgcaa tagtgagggg ctgcagtgca tgaacaccag 960
cacgagctac ctcagcaaga cgttatttga aattacagtg cctctctctc aaggccccaa 1020
accagtaaca atcagttttg ccaatcacac ttcctgccga tgcatgtcta aactggatgt 1080
ttacagacaa gttcattcca ttattagacg ttccctgcca gcaacactac cacagtgtca 1140
ggcagcgaac aagacctgcc ccaccaatta catgtggaat aatcacatct gcagatgcct 1200
ggctcaggaa gattttatgt tttcctcgga tgctggagat gactcaacag atggattcca 1260
tgacatctgt ggaccaaaca aggagctgga tgaagagacc tgtcagtgtg tctgcagagc 1320
ggggcttcgg cctgccagct gtggacccca caaagaacta gacagaaact catgccagtg 1380
tgtctgtaaa aacaaactct tccccagcca atgtggggcc aaccgagaat ttgatgaaaa 1440
cacatgccag tgtgtatgta aaagaacctg ccccagaaat caacccctaa atcctggaaa 1500
atgtgcctgt gaatgtacag aaagtccaca gaaatgcttg ttaaaaggaa agaagttcca 1560
ccaccaaaca tgcagctgtt acagacggcc atgtacgaac cgccagaagg cttgtgagcc 1620
aggattttca tatagtgaag aagtgtgtcg ttgtgtccct tcatattgga aaagaccaca 1680
aatgagctaa gattgtactg ttttccagtt catcgatttt ctattatgga aaactgtgtt 1740
gccacagtag aactgtctgt gaacagagag acccttgtgg gtccatgcta acaaagacaa 1800
aagtctgtct ttcctgaacc atgtggataa ctttacagaa atggactgga gctcatctgc 1860
aaaaggcctc ttgtaaagac tggttttctg ccaatgacca aacagccaag attttcctct 1920
tgtgatttct ttaaaagaat gactatataa tttatttcca ctaaaaatat tgtttctgca 1980
ttcattttta tagcaacaac aattggtaaa actcactgtg atcaatattt ttatatcatg 2040
caaaatatgt ttaaaataaa atgaaaattg tattat 2076

<210> 330
<211> 2819
<212> DNA
<213> Homo sapiens

<400> 330
ctgggcccag ctcccccgag aggtggtcgg atcctctggg ctgctcggtc gatgcctgtg 60
ccactgacgt ccaggcatga ggtggttcct gccctggacg ctggcagcag tgacagcagc 120
agccgccagc accgtcctgg ccacggccct ctctccagcc cctacgacca tggactttac 180
cccagctcca ctggaggaca cctcctcacg cccccaattc tgcaagtggc catgtgagtg 240
cccgccatcc ccacccccgct gcccgctggg ggtcagcctc atcacagatg gctgtgagtg 300
ctgtaagatg tgcgctcagc agcttgggga caactgcacg gaggctgcca tctgtgaccc 360
ccaccggggc ctctactgtg actacagcgg ggaccgcccg aggtacgcaa taggagtgtg 420
tgcacaggtg gtcggtgtgg gctgcgtcct ggatggggtg cgctacaaca acggccagtc 480
cttccagcct aactgcaagt acaactgcac gtgcatcgac ggcgcggtgg gctgcacacc 540
actgtgcctc cgagtgcgcc ccccgcgtct ctggtgcccc cacccgcggc gcgtgagcat 600
acctggccac tgctgtgagc agtgggtatg tgaggacgac gccaagaggc cacgcaagac 660
cgcaccccgt gacacaggag ccttcgatgc tgtgggtgag gtggaggcat ggcacaggaa 720
ctgcatagcc tacacaagcc cctggagccc ttgctccacc agctgcggcc tgggggtctc 780

cactcggatc tccaatgtta acgcccagtg ctggcctgag caagagagcc gcctctgcaa 840
cttgcggcca tgcgatgtgg acatccatac actcattaag gcagggaaga agtgtctggc 900
tgtgtaccag ccagaggcat ccatgaactt cacacttgcg ggctgcatca gcacacgctc 960
ctatcaaccc aagtactgtg gagtttgcat ggacaatagg tgctgcatcc cctacaagtc 1020
taagactatc gacgtgtcct tccagtgtcc tgatgggctt ggcttctccc gccaggtcct 1080
atggattaat gcctgcttct gtaacctgag ctgtaggaat cccaatgaca tctttgctga 1140
cttggaatcc taccctgact tctcagaaat tgccaactag gcaggcacaa atcttgggtc 1200
ttggggacta acccaatgcc tgtgaagcag tcagccctta tggccaataa cttttcacca 1260
atgagcctta gttaccctga tctggaccct tggcctccat ttctgtctct aaccattcaa 1320
atgacgcctg atggtgctgc tcaggcccat gctatgagtt ttctccttga tatcattcag 1380
catctactct aaagaaaaat gcctgtctct agctgttctg gactacaccc aagcctgatc 1440
cagcctttcc aagtcactag aagtcctgct ggatcttgcc taaatcccaa gaaatggaat 1500
caggtagact tttaatatca ctaatttctt ctttagatgc caaaccacaa gactctttgg 1560
gtccattcag atgaatagat ggaatttgga acaatagaat aatctattat ttggagcctg 1620
ccaagaggta ctgtaatggg taattctgac gtcagcgcac caaaactatc ctgattccaa 1680
atatgtatgc acctcaaggt catcaaacat ttgccaagtg agttgaatag ttgcttaatt 1740
ttgattttta atggaaagtt gtatccatta acctgggcat tgttgaggtt aagtttctct 1800
tcacccctac actgtgaagg gtacagatta ggtttgtccc agtcagaaat aaaatttgat 1860
aaacattcct gttgatggga aaagccccca gttaatactc cagagacagg gaaaggtcag 1920
cccgtttcag aaggaccaat tgactctcac actgaatcag ctgctgactg gcagggcttt 1980
gggcagttgg ccaggctctt ccttgaatct tctcccttgt cctgcttggg gttcatagga 2040
attggtaagg cctctggact ggcctgtctg gcccctgaga gtggtgccct ggaacactcc 2100
tctactctta cagagccttg agagacccag ctgcagacca tgccagaccc actgaaatga 2160
ccaagacagg ttcaggtagg ggtgtgggtc aaaccaagaa gtgggtgccc ttggtagcag 2220
cctggggtga cctctagagc tggaggctgt gggactccag gggcccccgt gttcaggaca 2280
catctattgc agagactcat ttcacagcct ttcgttctgc tgaccaaatg gccagttttc 2340
tggtaggaag atggaggttt accggttgtt tagaaacaga aatagactta ataaaggttt 2400
aaagctgaag aggttgaagc taaaaggaaa aggttgttgt taatgaatat caggctatta 2460
tttattgtat taggaaaata taatatttac tgttagaatt cttttattta gggccttttc 2520
tgtgccagac attgctctca gtgctttgca tgtattagct cactgaatct tcacgacaat 2580
gttgagaagt tcccattatt atttctgttc ttacaaatgt gaaacggaag ctcatagagg 2640
tgagaaaact caaccagagt cacccagttg gtgactggga aagttaggat tcagatcgaa 2700
attggactgt ctttataacc catattttcc ccctgttttt agagcttcca aatgtgtcag 2760
aataggaaaa cattgcaata aatggcttga tttttaaaa aaaaaaaaaa aaaaaaaaa 2819

<210> 331
<211> 2540
<212> DNA
<213> Homo sapiens

<400> 331
gaaaaggtgg acaagtccta ttttcaagag aagatgactt ttaacagttt tgaaggatct 60
aaaacttgtg tacctgcaga catcaataag gaagaagaat ttgtagaaga gtttaataga 120
ttaaaaactt ttgctaattt tccaagtggt agtcctgttt cagcatcaac actggcacga 180
gcagggtttc tttatactgg tgaaggagat accgtgcggt gctttagttg tcatgcagct 240
gtagatagat ggcaatatgg agactcagca gttggaagac acaggaaagt atccccaaat 300
tgcagattta tcaacggctt ttatcttgaa aatagtgcca cgcagtctac aaattctggt 360
atccagaatg gtcagtacaa agttgaaaac tatctgggaa gcagagatca ttttgcctta 420
gacaggccat ctgagacaca tgcagactat cttttgagaa ctgggcaggt tgtagatata 480
tcagacacca tatacccgag gaaccctgcc atgtattgtg aagaagctag attaaagtcc 540
tttcagaact ggccagacta tgctcaccta accccaagag agttagcaag tgctggactc 600
tactacacag gtattggtga ccaagtgcag tgcttttgtt gtggtggaaa actgaaaaat 660
tgggaacctt gtgatcgtgc ctggtcagaa cacaggcgac actttcctaa ttgcttcttt 720
gttttgggcc ggaatcttaa tattcgaagt gaatctgatg ctgtgagttc tgataggaat 780
ttcccaaatt caacaaatct tccaagaaat ccatccatgg cagattatga agcacggatc 840
tttacttttg ggacatggat atactcagtt aacaaggagc agcttgcaag agctggattt 900
tatgctttag gtgaaggtga taaagtaaag tgctttcact gtggaggagg gctaactgat 960
tggaagccca gtgaagaccc ttgggaacaa catgctaaat ggtatccagg gtgcaaatat 1020
ctgttagaac agaagggaca agaatatata aacaatattc atttaactca ttcacttgag 1080
gagtgtctgg taagaactac tgagaaaaca ccatcactaa ctagaagaat tgatgatacc 1140
atcttccaaa atcctatggt acaagaagct atacgaatgg ggttcagttt caaggacatt 1200
aagaaaataa tggaggaaaa aattcagata tctgggagca actataaatc acttgaggtt 1260
ctggttgcag atctagtgaa tgctcagaaa gacagtatgc aagatgagtc aagtcagact 1320
tcattacaga aagagattag tactgaagag cagctaaggc gcctgcaaga ggagaagctt 1380
tgcaaaatct gtatggatag aaatattgct atcgtttttg ttccttgtgg acatctagtc 1440
acttgtaaac aatgtgctga agcagttgac aagtgtccca tgtgctacac agtcattact 1500
ttcaagcaaa aaatttttat gtcttaatct aactctatag taggcatgtt atgttgttct 1560
tattaccctg attgaatgtg tgatgtgaac tgactttaag taatcaggat tgaattccat 1620

```
tagcatttgc taccaagtag gaaaaaaaat gtacatggca gtgttttagt tggcaatata 1680
atctttgaat ttcttgattt ttcagggtat tagctgtatt atccattttt tttactgtta 1740
tttaattgaa accatagact aagaataaga agcatcatac tataactgaa cacaatgtgt 1800
attcatagta tactgattta atttctaagt gtaagtgaat taatcatctg gatttttttat 1860
tcttttcaga taggcttaac aaatggagct ttctgtatat aaatgtggag attagagtta 1920
atctccccaa tcacataatt tgttttgtgt gaaaaaggaa taaattgttc catgctggtg 1980
gaaagataga gattgttttt agaggttggt tgttgtgttt taggattctg tccattttct 2040
tgtaaaggga taaacacgga cgtgtgcgaa atatgtttgt aaagtgattt gccattgttg 2100
aaagcgtatt taatgataga atactatcga gccaacatgt actgacatgg aaagatgtca 2160
gagatatgtt aagtgtaaaa tgcaagtggc gggacactat gtatagtctg agccagatca 2220
aagtatgtat gttgttaata tgcatagaac gagagatttg gaaagatata caccaaactg 2280
ttaaatgtgg tttctcttcg gggagggggg gattgggga ggggccccag aggggtttta 2340
gaggggcctt ttcactttcg actttttttca ttttgttctg ttcggatttt ttataagtat 2400
gtagaccccg aagggtttta tgggaactaa catcagtaac ctaacccccg tgactatcct 2460
gtgctcttcc tagggagctg tgttgtttcc cacccaccac ccttccctct gaacaaatgc 2520
ctgagtgctg gggcactttg                                             2540

<210> 332
<211> 1474
<212> DNA
<213> Homo sapiens

<400> 332
aaaaagaaat caagaatgca attttattta caatagtcac gccggaaata cctagaaata 60
aatttaactg aggatgtaaa agacctctac aaggagagtt caatgcgtag cgggagcgga 120
gagctgaccc cagagagccc tgggcagccc cacctccgcc gccggcctag ttaccatcac 180
accccggaga gcccgcagct gccgcagccg gccccagtca ccatcaccgc aaccatgagc 240
agcgaggccg agacccagca gccgcccgcc gcccccccg ccgcccccgc cctcagcgcc 300
gccgacacca agcccggcac taccggagcg gcgcagggag cggtggcccg ggcggctcac 360
atcggcggcg ctggcgcggg cgacaagaag gtcatcgcaa cgaaggtttt gggaacagta 420
aaatggttca atgtaaggaa cggatatggt ttcatcaaca ggaatgacac caaggaagat 480
gtatttgtac accagactgc cataaagaag aataacccca ggaagtacct tcgcagtgta 540
ggagatggag agactgtgga gtttgatgtt gttgaaggag aaaagggtgc ggaggcagca 600
aatgttacag gtcctggtgg tgttccagtt caaggcagta aatatgcagc agaccgtaac 660
cattatagac gctatccacg tcgtaggggt cctccacgca attaccagca aaattaccag 720
aatagtgaga gtggggaaaa gaacgaggga tcggagagtg ctcccgaagc caggcccaac 780
aacgccggcc ctacgcaggc gaaggttccc accttactac atgcggagac ctatgggcgt 840
cgaccacagt attccaaccc tcctgtgcag ggagaagtga tggagggtgc tgacaaccag 900
ggtgcaggag aacaaggtag accagtgagg cagatatgta tcggggatat agaccacgat 960
tccgcagggg ccctcctcgc caaaagacag cctagagagg acggcaatga agaagataaa 1020
gaaaatcaag gagatgagac ccaaggtcag cagccacctc aagctcggta ccgccgcaac 1080
ttcaattacc gacgcagacg cccagaaaac cctaaaccac aagatggcaa agagacaaaa 1140
gcagccgatc caccagctga gaattcgtcc gctcccgagg ctgagcaggg cggggctgag 1200
taaatgccgg cttaccatct ctaccatcat ccggtttagt catccaacaa gaagaaatat 1260
gaaattccag caataagaaa tgaacaaaag attggagctg aagacctaaa gtgcttgctt 1320
tttgcccgtt gaccagataa atagaactat ctgcattatc tatgcagcat ggggttttta 1380
ttatgtttta cctaaagacg tctcttttttg gtaataacaa accgtgtttt ttaaaaaagc 1440
ctggtttttc tcaatacgcc tttaaaggaa ttcc                             1474

<210> 333
<211> 4079
<212> DNA
<213> Homo sapiens

<400> 333
ggagcggcgg gcgggcggga gggctggcgg ggcgaacgtc tgggagacgt ctgaaagacc 60
aacgagactt tggagaccag agacgcgcct gggggggacct ggggcttggg gcgtgcgaga 120
tttcccttgc attcgctggg agctcgcgca gggatcgtcc catggccggg gctcggagcc 180
gcgacccttg gggggcctcc gggatttgct acctttttgg ctccctgctc gtcgaactgc 240
tcttctcacg ggctgtcgcc ttcaatctgg acgtgatggg tgccttgcgc aaggagggcg 300
agccaggcag cctcttcggc ttctctgtgg ccctgcaccg gcagttgcag ccccgacccc 360
agagctggct gctggtgggt gctccccagg ccctggctct tcctgggcag caggcgaatc 420
gcactggagg cctcttcgct tgcccgttga gcctggagga gactgactgc tacagagtgg 480
acatcgacca gggagctgat atgcaaaagg aaagcaagga gaaccagtgg ttgggagtca 540
gtgttcggag ccaggggcct gggggcaaga ttgttacctg tgcacaccga tatgaggcaa 600
ggcagcgagt ggaccagatc ctggagacgc gggatatgat tggtcgctgc tttgtgctca 660
gccaggacct ggccatccgg gatgagttgg atggtgggga atggaagttc tgtgagggac 720
gcccccaagg ccatgaacaa tttgggttct gccagcaggg cacagctgcc gccttctccc 780
```

ctgatagcca ctacctcctc tttggggccc caggaaccta taattggaag gggttgcttt 840
ttgtgaccaa cattgatagc tcagaccccg accagctggt gtataaaact ttggaccctg 900
ctgaccggct cccaggacca gccggagact tggccctcaa tagctactta ggcttctcta 960
ttgactcggg gaaaggtctg gtgcgtgcag aagagctgag ctttgtggct ggagcccccc 1020
gcgccaacca caagggtgct gtggttatcc tgcgcaagga cagcgccagt cgcctggtgc 1080
ccgaggttat gctgtctggg gagcgcctga cctccggctt tggctactca ctggctgtgg 1140
ctgacctcaa cagtgatggc tggccagacc tgatagtggg tgccccctac ttctttgagc 1200
gccaagaaga gctggggggt gctgtgtatg tgtacttgaa ccaggggggt cactgggctg 1260
ggatctcccc tctccggctc tgcggctccc ctgactccat gttcgggatc agcctggctg 1320
tcctggggga cctcaaccaa gatggctttc cagatattgc agtgggtgcc ccctttgatg 1380
gtgatgggaa agtcttcatc taccatggga gcagcctggg ggttgtcgcc aaaccttcac 1440
aggtgctgga gggcgaggct gtgggcatca agagcttcgg ctactccctg tcaggcagct 1500
tggatatgga tgggaaccaa taccctgacc tgctggtggg ctccctggct gacaccgcag 1560
tgctcttcag ggccagaccc atcctccatg tctcccatga ggtctctatt gctccacgaa 1620
gcatcgacct ggagcagccc aactgtgctg gcggccactc ggtctgtgtg gacctaaggg 1680
tctgtttcag ctacattgca gtccccagca gctatagccc tactgtggcc ctggactatg 1740
tgttagatgc ggacacagac cggaggctcc ggggccaggt tccccgtgtg acgttcctga 1800
gccgtaacct ggaagaaccc aagcaccagg cctcgggcac cgtgtggctg aagcaccagc 1860
atgaccgagt ctgtggagac gccatgttcc agctccagga aaatgtcaaa gacaagcttc 1920
gggccattgt agtgaccttg tcctacagtc tccagacccc tcggctccgg cgacaggctc 1980
ctggccaggg gctgcctcca gtggccccca tcctcaatgc ccaccagccc agcacccagc 2040
gggcagagat ccacttcctg aagcaaggct gtggtgaaga caagatctgc cagagcaatc 2100
tgcagctggt ccacgcccgc ttctgtaccc gggtcagcga cacggaattc caacctctgc 2160
ccatggatgt ggatggaaca acagccctgt ttgcactgag tgggcagcca gtcattggcc 2220
tggagctgat ggtcaccaac ctgccatcgg acccagccca gccccaggct gatggggatg 2280
atgcccatga agcccagctc ctggtcatgc ttcctgactc actgcactac tcaggggtcc 2340
gggccctgga ccctgcggag aagccactct gcctgtccaa tgagaatgcc tcccatgttg 2400
agtgtgagct ggggaacccc atgaagagag gtgcccaggt caccttctac ctcatcctta 2460
gcacctccgg gatcagcatt gagaccacgg aactggaggt agagctgctg ttggccacga 2520
tcagtgagca ggagctgcat ccagtctctg cacgagcccg tgtcttcatt gagctgccac 2580
tgtccattgc aggaatggcc attccccagc aactcttctt ctctggtgtg gtgaggggcg 2640
agagagccat gcagtctgag cgggatgtgg gcagcaaggt caagtatgag gtcacggttt 2700
ccaaccaagg ccagtcgctc agaaccctgg gctctgcctt cctcaacatc atgtggcctc 2760
atgagattgc caatgggaag tggttgctgt acccaatgca ggttgagctg gagggcgggc 2820
aggggcctgg gcagaaaggg ctttgctctc ccaggcccaa catcctccac ctggatgtgg 2880
acagtaggga taggaggcgg cgggagctgg agccacctga gcagcaggag cctggtgagc 2940
ggcaggagcc cagcatgtcc tggtggccag tgtcctctgc tgagaagaag aaaaacatca 3000
ccctggactg cgcccggggc acggccaact gtgtggtgtt cagctgccca ctctacagct 3060
ttgaccgcgc ggctgtgctg catgtctggg gccgtctctg gaacagcacc tttctggagg 3120
agtactcagc tgtgaagtcc ctggaagtga ttgtccgggc caacatcaca gtgaagtcct 3180
ccataaagaa cttgatgctc cgagatgcct ccacagtgat cccagtgatg gtatacttgg 3240
accccatggc tgtggtggca gaaggagtgc cctggtgggt catcctcctg gctgtactgg 3300
ctgggctgct ggtgctagca ctgctggtgc tgctcctgtg gaagatggga ttcttcaaac 3360
gggcgaagca ccccgaggcc accgtgcccc agtaccatgc ggtgaagatt cctcgggaag 3420
accgacagca gttcaaggag gagaagacgg gcaccatcct gaggaacaac tggggcagcc 3480
cccggcggga gggcccggat gcacacccca tcctggctgc tgacgggcat cccgagctgg 3540
gccccgatgg gcatccaggg ccaggcaccg cctaggttcc catgtcccag cctggcctgt 3600
ggctgccctc catcccttcc ccagagatgg ctccttggga tgaagagggt agagtgggct 3660
gctggtgtcg catcaagatt tggcaggatc ggcttcctca ggggcacaga cctctcccac 3720
ccacaagaac tcctcccacc caacttcccc ttagagtgct gtgagatgag agtgggtaaa 3780
tcagggacag ggccatgggg tagggtgaga agggcagggg tgtcctgatg caaaggtggg 3840
gagaagggat cctaatccct tcctctccca ttcaccctgt gtaacaggac cccaaggacc 3900
tgcctccccg gaagtgcctt aacctagagg gtcggggagg aggttgtgtc actgactcag 3960
gctgctcctt ctctagtttc ccctctcatc tgaccttagt ttgctgccat cagtctagtg 4020
gtttcgtggt ttcgtctatt tattaaaaaa tatttgagaa caaaaaaaaa aaaaaaaaa 4079

<210> 334
<211> 3373
<212> DNA
<213> Homo sapiens

<400> 334
ggtggcaact tctcctcctg cggccgggag cggcctgcct gcctccctgc gcacccgcag 60
cctcccccgc tgcctcccta gggctcccct ccggccgcca gcgcccattt ttcattccct 120
agatagagat actttgcgcg cacacacata catacgcgcg caaaaaggaa aaaaaaaaaa 180
aaaagcccac cctccagcct cgctgcaaag agaaaaccgg agcagccgca gctcgcagct 240
cgcagctcgc agcccgcagc ccgcagagga cgcccagagc ggcgagcagg cgggcagacg 300
gaccgacgga ctcgcgccgc gtccacctgt cggccgggcc cagccgagcg cgcagcgggc 360

```
acgccgcgcg cgcggagcag ccgtgcccgc cgcccgggcc cgccgccagg gcgcacacgc 420
tcccgccccc ctacccggcc cgggcgggag tttgcacctc tccctgcccg ggtgctcgag 480
ctgccgttgc aaagccaact ttggaaaaag tttttggggg gagacttggg ccttgaggtg 540
cccagctccg cgctttccga ttttgggggc ctttccagaa aatgttgcaa aaaagctaag 600
ccggcgggca gaggaaaacg cctgtagccg gcgagtgaag acgaaccatc gactgccgtg 660
ttcctttttcc tcttggaggt tggagtcccc tgggcgcccc cacacggcta gacgcctcgg 720
ctggttcgcg acgcagcccc ccggccgtgg atgctgcact cgggctcggg atccgcccag 780
gtagccggcc tcggacccag gtcctgcgcc caggtcctcc cctgcccccc agcgacggag 840
ccggggccgg gggcggcggc gccgggggca tgcgggtgag ccgcggctgc agaggcctga 900
gcgcctgatc gccgcggacc tgagccgagc ccaccccccct ccccagcccc ccaccctggc 960
cgcgggggcg gcgcgctcga tctacgcgtc cggggccccg cggggccggg cccggagtcg 1020
gcatgaatcg ctgctgggcg ctcttcctgt ctctctgctg ctacctgcgt ctggtcagcg 1080
ccgaggggga ccccattccc gaggagcttt atgagatgct gagtgaccac tcgatccgct 1140
cctttgatga tctccaacgc ctgctgcacg gagaccccgg agaggaagat ggggccgagt 1200
tggacctgaa catgacccgc tcccactctg gaggcgagct ggagagcttg gctcgtggaa 1260
gaaggagcct gggttccctg accattgctg agccggccat gatcgccgag tgcaagacgc 1320
gcaccgaggt gttcgagatc tcccggcgcc tcatagaccg caccaacgcc aacttcctgg 1380
tgtggccgcc ctgtgtggag gtgcagcgct gctccggctg ctgcaacaac cgcaacgtgc 1440
agtgccgcccc cacccaggtg cagctgcgac ctgtccaggt gagaaagatc gagattgtgc 1500
ggaagaagcc aatctttaag aaggccacgg tgacgctgga agaccacctg gcatgcaagt 1560
gtgagacagt ggcagctgca cggcctgtga cccgaagccc gggggttcc caggagcagc 1620
gagccaaaac gccccaaact cgggtgacca ttcggacggt gcgagtccgc cggcccccca 1680
agggcaagca ccggaaattc aagcacacgc atgacaagac ggcactgaag gagaccttg 1740
gagcctaggg gcatcggcag gagagtgtgt gggcagggtt atttaatatg gtatttgctg 1800
tattgccccc atggggtcct tggagtgata atattgtttc cctcgtccgt ctgtctcgat 1860
gcctgattcg gacggccaat ggtgcttccc ccacccctcc acgtgtccgt ccacccttcc 1920
atcagcgggt ctcctcccag cggcctccgg tcttgcccag cagctcaaag aagaaaaaga 1980
aggactgaac tccatcgcca tcttcttccc ttaactccaa gaacttggga taagagtgtg 2040
agagagactg atggggtcgc tctttggggg aaacgggttc cttcccctgc acctggcctg 2100
ggccacacct gagcgctgtg gactgtcctg aggagccctg aggacctctc agcatagcct 2160
gcctgatccc tgaacccctg gccagctctg aggggaggca cctccaggca ggccaggctg 2220
cctcggactc catggctaag accacagacg ggcacacaga ctggagaaaa cccctcccac 2280
ggtgcccaaa caccagtcac ctcgtctccc tggtgcctct gtgcacagtg gcttcttttc 2340
gttttcgttt tgaagacgtg gactcctctt ggtgggtgtg gccagcacac caagtggctg 2400
ggtgccctct caggtgggtt agagatggag tttgctgttg aggtggtgta gatggtgacc 2460
tgggtatccc ctgcctcctg ccacccttc ctccccatac tccactctga ttcacctctt 2520
cctctggttc ctttcatctc tctacctcca ccctgcattt tcctcttgtc ctggcccttc 2580
agtctgctcc accaaggggc tcttgaaccc cttattaagg ccccagatga ccccagtcac 2640
tcctctctag ggcagaagac tagaggccag ggcagcaagg gacctgctca tcatattcca 2700
acccagccac gactgccatg taaggttgtg cagggtgtgt actgcacaag gacattgtat 2760
gcagggagca ctgttcacat catagataaa gctgatttgt atatttatta tgacaatttc 2820
tggcagatgt aggtaaagag gaaaaggatc cttttcctaa ttcacacaaa gactccttgt 2880
ggactggctg tgcccctgat gcagcctgtg gctggagtgg ccaaatagga gggagactgt 2940
ggtaggggca gggaggcaac actgctgtcc acatgacctc catttcccaa agtcctctgc 3000
tccagcaact gcccttccag gtgggtgtgg gacacctggg agaaggtctc caagggaggg 3060
tgcagccctc ttgcccgcac ccctccctgc ttgcacactt ccccatcttt gatccttctg 3120
agctccacct ctggtggctc ctcctaggaa accagctcgt gggctgggaa tgggggagag 3180
aagggaaaag atccccaaga ccccctgggg tgggatctga gctcccacct cccttcccac 3240
ctactgcact ttccccttc ccgccttcca aaacctgctt ccttcagttt gtaaagtcgg 3300
tgattatatt tttgggggct ttcctttttat tttttaaatg taaaatttat ttatattccg 3360
tatttaaagt tgt 3373
```

<210> 335
<211> 2304
<212> DNA
<213> Homo sapiens

<400> 335

```
gtccccgcag cgccgtcgcg ccctcctgcc gcaggccacc gaggccgccg ccgtctagcg 60
ccccgacctc gccaccatga gagccctgct ggcgcgcctg cttctctgcg tcctggtcgt 120
gagcgactcc aaaggcagca atgaacttca tcaagttcca tcgaactgtg actgtctaaa 180
tggaggaaca tgtgtgtcca acaagtactt ctccaacatt cactggtgca actgcccaaa 240
gaaattcgga gggcagcact gtgaaataga taagtcaaaa acctgctatg aggggaatgg 300
tcacttttac cgaggaaagg ccagcactga caccatgggc cggccctgcc tgccctggaa 360
ctctgccact gtccttcagc aaacgtacca tgcccacaga tctgatgctc ttcagctggg 420
cctggggaaa cataattact gcaggaaccc agacaaccgg aggcgaccct ggtgctatgt 480
gcaggtgggc ctaaagccgc ttgtccaaga gtgcatggtg catgactgcg cagatggaaa 540
aaagccctcc tctcctccag aagaattaaa atttcagtgt ggccaaaaga ctctgaggcc 600
```

```
ccgctttaag attattgggg gagaattcac caccatcgag aaccagccct ggtttgcggc 660
catctacagg aggcaccggg ggggctctgt cacctacgtg tgtggaggca gcctcatcag 720
cccttgctgg gtgatcagcg ccacacactg cttcattgat tacccaaaga aggaggacta 780
catcgtctac ctgggtcgct caaggcttaa ctccaacacg caaggggaga tgaagtttga 840
ggtggaaaac ctcatcctac acaaggacta cagcgctgac acgcttgctc accacaacga 900
cattgccttg ctgaagatcc gttccaagga gggcaggtgt gcgcagccat cccggactat 960
acagaccatc tgcctgccct cgatgtataa cgatccccag tttggcacaa gctgtgagat 1020
cactggcttt ggaaaagaga attctaccga ctatctctat ccggagcagc tgaaaatgac 1080
tgttgtgaag ctgatttccc accgggagtg tcagcagccc cactactacg gctctgaagt 1140
caccaccaaa atgctatgtg ctgctgaccc ccaatggaaa acagattcct gccagggaga 1200
ctcaggggga cccctcgtct gttccctcca aggccgcatg actttgactg gaattgtgag 1260
ctggggccgt ggatgtgccc tgaaggacaa gccaggcgtc tacacgagag tctcacactt 1320
cttaccctgg atccgcagtc acaccaagga agagaatggc ctggccctct gagggtcccc 1380
agggaggaaa cgggcaccac ccgctttctt gctggttgtc atttttgcag tagagtcatc 1440
tccatcagct gtaagaagag actgggaaga taggctctgc acagatggat ttgcctgtgg 1500
caccaccagg gtgaacgaca atagctttac cctcacggat aggcctgggt gctggctgcc 1560
cagaccctct ggccaggatg gaggggtggt cctgactcaa catgttactg accagcaact 1620
tgtctttttc tggactgaag cctgcaggag ttaaaaaggg cagggcatct cctgtgcatg 1680
ggctcgaagg gagagccagc tcccccgacc ggtgggcatt tgtgaggccc atggttgaga 1740
aatgaataat ttcccaatta ggaagtgtaa gcagctgagg tctcttgagg gagcttagcc 1800
aatgtgggag cagcggtttg gggagcagag acactaacga cttcagggca gggctctgat 1860
attccatgaa tgtatcagga aatatatatg tgtgtgtatg tttgcacact tgttgtgtgg 1920
gctgtgagtg taagtgtgag taagagctgg tgtctgattg ttaagtctaa atatttcctt 1980
aaactgtgtg gactgtgatg ccacacagag tggtctttct ggagaggtta taggtcactc 2040
ctggggcctc ttgggtcccc cacgtgacag tgcctgggaa tgtacttatt ctgcagcatg 2100
acctgtgacc agcactgtct cagtttcact ttcacataga tgtccctttc ttggccagtt 2160
atccccttcct tttagcctag ttcatccaat cctcactggg tggggtgagg accactcctt 2220
acactgaata tttatatttc actattttta tttatatttt tgtaatttta aataaaagtg 2280
atcaataaaa tgtgattttt ctga 2304
```

<210> 336
<211> 1876
<212> DNA
<213> Homo sapiens

<400> 336

```
cgcggccgcg gttcgctgtg gcgggcgcct gggccgccgg ctgtttaact tcgcttccgc 60
tggcccatag tgatctttgc agtgacccag cagcatcact gtttcttggc gtgtgaagat 120
aacccaagga attgaggaag ttgctgagaa gagtgtgctg gagatgctct aggaaaaaat 180
tgaatagtga gacgagttcc agcgcaaggg tttctggttt gccaagaaga aagtgaacat 240
catggatcag aacaacagcc tgccacctta cgctcagggc ttggcctccc ctcagggtgc 300
catgactccc ggaatcccta tctttagtcc aatgatgcct tatggcactg gactgacccc 360
acagcctatt cagaacacca atagtctgtc tattttggaa gagcaacaaa ggcagcagca 420
gcaacaacaa cagcagcagc agcagcagca gcagcagcaa cagcaacagc agcagcagca 480
gcagcagcag cagcagcagc agcagcagca gcagcagcag caacaggcag tggcagctgc 540
agccgttcag cagtcaacgt cccagcaggc aacacaggga acctcaggcc aggcaccaca 600
gctcttccac tcacagactc tcacaactgc acccttgccg ggcaccactc cactgtatcc 660
ctcccccatg actcccatga cccccatcac tcctgccacg ccagcttcgg agagttctgg 720
gattgtaccg cagctgcaaa atattgtatc cacagtgaat cttggttgta aacttgacct 780
aaagaccatt gcacttcgtg cccgaaacgc cgaatataat cccaagcggt ttgctgcggt 840
aatcatgagg ataagagagc cacgaaccac ggcactgatt ttcagttctg ggaaaatggt 900
gtgcacagga gccaagagtg aagaacagtc cagactggca gcaagaaaat atgctagagt 960
tgtacagaag ttgggttttc cagctaagtt cttggacttc aagattcaga acatggtggg 1020
gagctgtgat gtgaagtttc ctataaggtt agaaggcctt gtgctcaccc accaacaatt 1080
tagtagttat gagccagagt tatttcctgg tttaatctac agaatgatca aacccagaat 1140
tgttctcctt atttttgttt ctggaaaagt tgtattaaca ggtgctaaag tcagagcaga 1200
aatttatgaa gcatttgaaa acatctaccc tattctaaag ggattcagga agacgacgta 1260
atggctctca tgtacccttg cctcccccac ccccttcttt tttttttttt aaacaaatca 1320
gtttgttttg gtaccttaa atggtggtgt tgtgagaaga tggatgttga gttgcagggt 1380
gtggcaccag gtgatgccct tctgtaagtg ccccaccgcgg gatgccggga aggggcatta 1440
tttgtgcact gagaacaccg cgcagcgtga ctgtgagttg ctcataccgt gctgctatct 1500
gggcagcgct gcccatttat ttatatgtag attttaaaca ctgctgttga caagttggtt 1560
tgagggagaa aactttaagt gttaaagcca cctctataat tgattggact ttttaatttt 1620
aatgtttttc cccatgaacc acagttttta tatttctacc agaaaagtaa aaatcttttt 1680
taaaagtgtt gtttttctaa tttataactc ctaggggtta tttctgtgcc agacacattc 1740
cacctctcca gtattgcagg acggaatata tgtgttaatg aaaatgaatg gctgtacata 1800
tttttttctt tcttcagagt actctgtaca ataaatgcag tttataaaag tgttaaaaaa 1860
aaaaaaaaaa aaaaaa 1876
```

<210> 337
<211> 6633
<212> DNA
<213> Homo sapiens

<400> 337
ttctccccgc cccccagttg ttgtcgaagt ctggggggttg ggactggacc ccctgattgc 60
gtaagagcaa aaagcgaagg cgcaatctgg acactgggag attcggagcg cagggagttt 120
gagagaaact tttattttga agagaccaag gttgaggggg ggcttatttc ctgacagcta 180
tttacttaga gcaaatgatt agttttagaa ggatggacta taacattgaa tcaattacaa 240
aacgcggttt ttgagcccat tactgttgga gctacaggga gagaaacagg aggagactgc 300
aagagatcat ttgggaaggc cgtgggcacg ctctttactc catgtgtggg acattcattg 360
cggaataaca tcggaggaga agtttcccag agctatgggg acttcccatc cggcgttcct 420
ggtcttaggc tgtcttctca cagggctgag cctaatcctc tgccagcttt cattaccctc 480
tatccttcca aatgaaaatg aaaaggttgt gcagctgaat tcatcctttt ctctgagatg 540
ctttggggag agtgaagtga gctggcagta ccccatgtct gaagaagaga gctccgatgt 600
ggaaatcaga aatgaagaaa acaacagcgg cctttttgtg acggtcttgg aagtgagcag 660
tgcctcggcg gcccacacag ggttgtacac ttgctattac aaccacactc agacagaaga 720
gaatgagctt gaaggcaggc acatttacat ctatgtgcca gacccagatg tagcctttgt 780
acctctagga atgacggatt atttagtcat cgtggaggat gatgattctg ccattatacc 840
ttgtcgcaca actgatcccg agactcctgt aaccttacac aacagtgagg gggtggtacc 900
tgcctcctac gacagcagac agggctttaa tgggaccttc actgtagggc cctatatctg 960
tgaggccacc gtcaaaggaa agaagttcca gaccatccca tttaatgttt atgctttaaa 1020
agcaacatca gagctggatc tagaaatgga agctcttaaa accgtgtata agtcagggga 1080
aacgattgtg gtcacctgtg ctgtttttaa caatgaggtg gttgaccttc aatggactta 1140
ccctggagaa gtgaaaggca aaggcatcac aatgctggaa gaaatcaaag tcccatccat 1200
caaattggtg tacactttga cggtccccga ggccacggtg aaagacagtg gagattacga 1260
atgtgctgcc cgccaggcta ccagggaggt caaagaaatg aagaaagtca ctatttctgt 1320
ccatgagaaa ggtttcattg aaatcaaacc caccttcagc cagttggaag ctgtcaacct 1380
gcatgaagtc aaacattttg ttgtagaggt gcgggcctac ccacctccca ggatatcctg 1440
gctgaaaaac aatctgactc tgattgaaaa tctcactgag atcaccactg atgtggaaaa 1500
gattcaggaa ataaggtatc gaagcaaatt aaagctgatc cgtgctaagg aagaagacag 1560
tggccattat actattgtag ctcaaaatga agatgctgtg aagagctata cttttgaact 1620
gttaactcaa gttccttcat ccattctgga cttggtcgat gatcaccatg gctcaactgg 1680
gggacagacg gtgaggtgca cagctgaagg cacgccgctt cctgatattg agtggatgat 1740
atgcaaagat attaagaaat gtaataatga aacttcctgg actattttgg ccaacaatgt 1800
ctcaaacatc atcacggaga tccactcccg agacaggagt accgtggagg gccgtgtgac 1860
tttcgccaaa gtggaggaga ccatcgccgt gcgatgcctg gctaagaatc tccttggagc 1920
tgagaaccga gagctgaagc tggtggctcc caccctgcgt tctgaactca cggtggctgc 1980
tgcagtcctg gtgctgttgg tgattgtgat catctcactt attgtcctgg ttgtcatttg 2040
gaaacagaaa ccgaggtatg aaattcgctg gagggtcatt gaatcaatca gcccggatgg 2100
acatgaatat atttatgtgg acccgatgca gctgccttat gactcaagat gggagtttcc 2160
aagagatgga ctagtgcttg gtcgggtctt ggggtctgga gcgtttggga aggtggttga 2220
aggaacagcc tatggattaa gccggtccca acctgtcatg aaagttgcag tgaagatgct 2280
aaaacccacg gccagatcca gtgaaaaaca agctctcatg tctgaactga agataatgac 2340
tcacctgggg ccacatttga acattgtaaa cttgctggga gcctgcacca agtcaggccc 2400
catttacatc atcacagagt attgcttcta tggagatttg gtcaactatt tgcataagaa 2460
tagggatagc ttcctgagcc accacccaga gaagccaaag aaagagctgg atatctttgg 2520
attgaaccct gctgatgaaa gcacacggag ctatgttatt ttatcttttg aaaacaatgg 2580
tgactacatg gacatgaagc aggctgatac tacacagtat gtccccatgc tagaaaggaa 2640
agaggtttct aaatattccg acatccagag atcactctat gatcgtccag cctcatataa 2700
gaagaaatct atgttagact cagaagtcaa aaacctcctt tcagatgata actcagaagg 2760
ccttacttta ttggatttgt tgagcttcac ctatcaagtt gcccgaggaa tggagttttt 2820
ggcttcaaaa aattgtgtcc accgtgatct ggctgctcgc aacgtcctcc tggcacaagg 2880
aaaaattgtg aagatctgtg actttggcct ggccagagac atcatgcatg attcgaacta 2940
tgtgtcgaaa ggcagtacct ttctgcccgt gaagtggatg gctcctgaga gcatctttga 3000
caacctctac accacactga gtgatgtctg gtcttatggc attctgctct gggagatctt 3060
ttcccttggt ggcacccctt accccggcat gatggtggat tctactttct acaataagat 3120
caagagtggg taccggatgg ccaagcctga ccacgctacc agtgaagtct acgagatcat 3180
ggtgaaatgc tggaacagtg agccggagaa gagaccctcc ttttaccacc tgagtgagat 3240
tgtggagaat ctgctgcctg gacaatataa aaagagttat gaaaaaattc acctggactt 3300
cctgaagagt gaccatcctg ctgtggcacg catgcgtgtg gactcagaca atgcatacat 3360
tggtgtcacc tacaaaaacg aggaagacaa gctgaaggac tgggagggtg gtctggatga 3420
gcagagactg agcgctgaca gtggctacat cattcctctg cctgacattg accctgtccc 3480
tgaggaggag gacctgggca agaggaacag acacagctcg cagacctctg aagagagtgc 3540
cattgagacg ggttccagca gttccacctt catcaagaga gaggacgaga ccattgaaga 3600
catcgacatg atggacgaca tcggcataga ctcttcagac ctggtggaag acagcttcct 3660

gtaactggcg gattcgaggg gttccttcca cttctggggc cacctctgga tcccgttcag 3720
aaaaccactt tattgcaatg cggaggttga gaggaggact tggttgatgt ttaaagagaa 3780
gttcccagcc aagggcctcg gggagcgttc taaatatgaa tgaatgggat attttgaaat 3840
gaactttgtc agtgttgcct ctcgcaatgc ctcagtagca tctcagtggt gtgtgaagtt 3900
tggagataga tggataaggg aataataggc cacagaaggt gaactttgtg cttcaaggac 3960
attggtgaga gtccaacaga cacaatttat actgcgacag aacttcagca ttgtaattat 4020
gtaaataact ctaaccaagg ctgtgtttag attgtattaa ctatcttctt tggacttctg 4080
aagagaccac tcaatccatc catgtacttc cctcttgaaa cctgatgtca gctgctgttg 4140
aactttttaa agaagtgcat gaaaaaccat ttttgaacct taaaaggtac tggtactata 4200
gcattttgct atctttttta gtgttaagag ataaagaata ataattaacc aaccttgttt 4260
aatagatttg ggtcatttag aagcctgaca actcattttc atattgtaat ctatgtttat 4320
aatactacta ctgttatcag taatgctaaa tgtgtaataa tgtaacatga tttccctcca 4380
gagaaagcac aatttaaaac aatccttact aagtaggtga tgagtttgac agtttttgac 4440
atttatatta aataacatgt ttctctataa agtatggtaa tagctttagt gaattaaatt 4500
tagttgagca tagagaacaa agtaaaagta gtgttgtcca ggaagtcaga atttttaact 4560
gtactgaata ggttccccaa tccatcgtat taaaaaacaa ttaactgccc tctgaaataa 4620
tgggattaga aacaaacaaa actcttaagt cctaaaagtt ctcaatgtag aggcataaac 4680
ctgtgctgaa cataacttct catgtatatt acccaatgga aaatataatg atcagcaaaa 4740
agactggatt tgcagaagtt tttttttttt ttcttcatgc ctgatgaaag ctttggcaac 4800
cccaatatat gtattttttg aatctatgaa cctgaaaagg gtcagaagga tgcccagaca 4860
tcagcctcct tctttcaccc cttaccccaa agagaaagag tttgaaactc gagaccataa 4920
agatattctt tagtggaggc tggatgtgca ttagcctgga tcctcagttc tcaaatgtgt 4980
gtggcagcca ggatgactag atcctgggtt tccatccttg agattctgaa gtatgaagtc 5040
tgagggaaac cagagtctgt atttttctaa actccctggc tgttctgatc ggccagtttt 5100
cggaaacact gacttaggtt tcaggaagtt gccatgggaa acaaataatt tgaactttgg 5160
aacagggttg gaattcaacc acgcaggaag cctactattt aaatccttgg cttcaggtta 5220
gtgacattta atgccatcta gctagcaatt gcgaccttaa tttaactttc cagtcttagc 5280
tgaggctgag aaagctaaag tttggttttg acaggtttc caaaagtaaa gatgctactt 5340
cccactgtat gggggagatt gaactttccc cgtctcccgt cttctgcctc ccactccata 5400
ccccgccaag gaaaggcatg tacaaaaatt atgcaattca gtgttccaag tctctgtgta 5460
accagctcag tgttttggtg gaaaaaacat tttaagtttt actgataatt tgaggttaga 5520
tgggaggatg aattgtcaca tctatccaca ctgtcaaaca ggttggtgtg ggttcattgg 5580
cattctttgc aatactgctt aattgctgat accatatgaa tgaaacatgg gctgtgatta 5640
ctgcaatcac tgtgctatcg gcagatgatg ctttggaaga tgcagaagca ataataaagt 5700
acttgactac ctactggtgt aatctcaatg caagccccaa ctttcttatc caacttttc 5760
atagtaagtg cgaagactga gccagattgg ccaattaaaa acgaaaacct gactaggttc 5820
tgtagagcca attagacttg aaatacgttt gtgtttctag aatcacagct caagcattct 5880
gtttatcgct cactctccct tgtacagcct tattttgttg gtgctttgca ttttgatatt 5940
gctgtgagcc ttgcatgaca tcatgaggcc ggatgaaact tctcagtcca gcagtttcca 6000
gtcctaacaa atgctcccac ctgaatttgt atatgactgc atttgtgggt gtgtgtgtgt 6060
tttcagcaaa ttccagattt gtttcctttt ggcctcctgc aaagtctcca gaagaaaatt 6120
tgccaatctt tcctactttc tatttttatg atgacaatca aagccggcct gagaaacact 6180
atttgtgact ttttaaacga ttagtgatgt ccttaaaatg tggtctgcca atctgtacaa 6240
aatggtccta tttttgtgaa gagggacata agataaaatg atgttataca tcaatatgta 6300
tatatgtatt tctatataga cttggagaat actgccaaaa catttatgac aagctgtatc 6360
actgccttcg tttatatttt tttaactgtg ataatcccca caggcacatt aactgttgca 6420
cttttgaatg tccaaaattt atattttaga aataataaaa agaaagatac ttacatgttc 6480
ccaaaacaat ggtgtggtga atgtgtgaga aaaactaact tgatagggtc taccaataca 6540
aaatgtatta cgaatgcccc tgttcatgtt tttgttttaa aacgtgtaaa tgaagatctt 6600
tatatttcaa taaatgatat ataatttaaa gtt 6633

<210> 338
<211> 994
<212> DNA
<213> Homo sapiens

<400> 338
tgctggccag cacctcgagg gaagatggcg gacgaggaga agctgccgcc cggctgggag 60
aagcgcatga gccgcagctc aggccgagtg tactacttca accacatcac taacgccagc 120
cagtgggagc ggcccagcgg caacagcagc agtggtggca aaaacgggca gggggagcct 180
gccagggtcc gctgctcgca cctgctggtg aagcacagcc agtcacggcg gccctcgtcc 240
tggcggcagg agaagatcac ccggaccaag gaggaggccc tggagctgat caacggctac 300
atccagaaga tcaagtcggg agaggaggac tttgagtctc tggcctcaca gttcagcgac 360
tgcagctcag ccaaggccag gggagacctg ggtgccttca gcagaggtca gatgcagaag 420
ccatttgaag acgcctcgtt tgcgctgcgg acgggggaga tgagcgggcc cgtgttcacg 480
gattccggca tccacatcat cctccgcact gagtgagggt ggggagccca ggcctggcct 540

cggggcaggg cagggcggct aggccggcca gctcccctt gcccgccagc cagtggccga 600
accccccact ccctgccacc gtcacacagt atttattgtt cccacaatgg ctgggagggg 660
gcccttccag attgggggcc ctggggtccc cactccctgt ccatccccag ttggggctgc 720
gaccgccaga ttctccctta aggaattgac ttcagcaggg gtgggaggct cccagaccca 780
gggcagtgtg gtgggagggg tgttccaaag agaaggcctg gtcagcagag ccgccccgtg 840
tccccccagg tgctggaggc agactcgagg gccgaattgt ttctagttag gccacgctcc 900
tctgttcagt cgcaaaggtg aacactcatg cggcagccat gggccctctg agcaactgtg 960
cagacccttt cacccccaat taaacccaga acca 994

<210> 339
<211> 772
<212> DNA
<213> Homo sapiens

<400> 339
agctcgtgcc gaattcggca cgagccgggt cggagccatg gcggtggcaa attcaagtcc 60
tgttaacccc gtggtgttct ttgatgtcag tattggcggt caggaagttg gccgcatgaa 120
gatcgagctc tttgcagacg ttgtgcctaa gacggccgag aactttaggc agttctgcac 180
cggagaattc aggaaagatg ggttccaat aggatacaaa ggaagcacct tccacagggt 240
cataaaggat ttcatgattc agggtggaga ttttgttaat ggagatggta ctggagtcgc 300
cagtatttac cggggggccat ttgcagatga aaattttaaa cttagacact cagctccagg 360
cctgctttcc atggcgaaca gtggtccaag tacaaatggc tgtcagttct ttatcacctg 420
ctctaagtgc gattggctgg atgggaagca tgtggtgttt ggaaaaatca tcgatggact 480
tctagtgatg agaaagattg agaatgttcc cacaggcccc aacaataagc ccaagctacc 540
tgtggtgatc tcgcagtgtg gggagatgta gtccagacaa agactgaatc aggccttccc 600
ttcttcttgg tggtgttctt gagtaagata atctggactg gcccccgtct ttgcttccct 660
gcctgctgct gccccatttg atcaagagac catggaagtg tcagagattc agaatccaag 720
attgtcttta agttttcaac tgtaaataaa gttttttgt atgcgtaaaa aa 772

<210> 340
<211> 919
<212> DNA
<213> Homo sapiens

<400> 340
cgctcgcctc cctcgctcca cgcgcgcccg gacgcggcgg ccaggcttgc gcgtggttcc 60
cctcccggtg ggcggattcc tgggcaagat gaagtgggtg tgggcgctct tgctgttggc 120
ggcgtgggca gcggccgagc gcgactgccg agtgagcagc ttccgagtca aggagaactt 180
cgacaaggct cgcttctctg ggacctggta cgccatggcc aagaaggacc ccgagggcct 240
ctttctgcag gacaacatcg tcgcggagtt ctcggtggac gagaccggcc agatgagcgc 300
cacagccaag ggccgagtcc gtcttttgaa taactgggac gtgtgcgcag acatggtggg 360
caccttcaca gacaccgagg accctgccaa gttcaagatg aagtactggg gcgtagcctc 420
ctttctgcag aaaggaaatg atgaccactg gatcgtcgac acagactacg acacgtatgc 480
cgtacagtac tcctgccgcc tcctgaacct cgatggcacc tgtgctgaca gctactcctt 540
cgtgttttcc cgggacccca acggcctgcc cccagaagcg cagaagattg taaggcagcg 600
gcaggaggag ctgtgcctgg ccaggcagta caggctgatc gtccacaacg gttactgcga 660
tggcagatca gaaagaaacc ttttgtagca atatcaagaa tctagtttca tctgagaact 720
tctgattagc tctcagtctt cagctctatt tatcttagga gtttaatttg cccttctctc 780
cccatcttcc ctcagttccc ataaaacctt cattacacat aaagatacac gtgggggtca 840
gtgaatctgc ttgcctttcc tgaaagtttc tggggcttaa gattccagac tctgattcat 900
taaactatag tcacccgtg 919

<210> 341
<211> 7365
<212> DNA
<213> Homo sapiens

<400> 341
ggcagtttgt aggtcgcgag ggaagcgctg aggatcagga agggggcact gagtgtccgt 60
gggggaatcc tcgtgatagg aactggaata tgccttgagg gggacactat gtctttaaaa 120
acgtcggctg gtcatgaggt caggagttcc agaccagcct gaccaacgtg gtgaaactcc 180
gtctctacta aaaatacaaa aattagccgg gcgtggtgcc gctccagcta ctcaggaggc 240
tgaggcagga gaatcgctag aacccgggag gcggaggttg cagtgagccg agatcgcgcc 300
attgcactcc agcctgggcg acagagcgag actgtctcaa aacaaaacaa aacaaaacaa 360
aacaaaaaac accggctgtt cattggaaca gaaagaaatg gatttatctg ctcttcgcgt 420
tgaagaagta caaaatgtca ttaatgctat gcagaaaatc ttagagtgtc ccatctgtct 480
ggagttgatc aaggaacctg tctccacaaa gtgtgaccac atattttgca aattttgcat 540
gctgaaactt ctcaaccaga agaaagggcc ttcacagtgt cctttatgta agaatgatat 600

aaccaaaagg agcctacaag aaagtacgag atttagtcaa cttgttgaag agctattgaa 660
aatcatttgt gcttttcagc ttgacacagg tttggagtat gcaaacagct ataattttgc 720
aaaaaaggaa aataactctc ctgaacatct aaaagatgaa gtttctatca tccaaagtat 780
gggctacaga aaccgtgcca aaagacttct acagagtgaa cccgaaaatc cttccttgca 840
ggaaaccagt ctcagtgtcc aactctctaa ccttggaact gtgagaactc tgaggacaaa 900
gcagcggata caacctcaaa agacgtctgt ctacattgaa ttgggatctg attcttctga 960
agataccgtt aataaggcaa cttattgcag tgtgggagat caagaattgt tacaaatcac 1020
ccctcaagga accagggatg aaatcagttt ggattctgca aaaaaggctg cttgtgaatt 1080
ttctgagacg gatgtaacaa atactgaaca tcatcaaccc agtaataatg atttgaacac 1140
cactgagaag cgtgcagctg agaggcatcc agaaaagtat cagggtagtt ctgtttcaaa 1200
cttgcatgtg gagccatgtg gcacaaatac tcatgccagc tcattacagc atgagaacag 1260
cagtttatta ctcactaaag acagaatgaa tgtagaaaag gctgaattct gtaataaaag 1320
caaacagcct ggcttagcaa ggagccaaca taacagatgg gctggaagta aggaaacatg 1380
taatgatagg cggactccca gcacagaaaa aaaggtagat ctgaatgctg atcccctgtg 1440
tgagagaaaa gaatggaata agcagaaact gccatgctca gagaatccta gagatactga 1500
agatgttcct tggataacac taaatagcag cattcagaaa gttaatgagt ggttttccag 1560
aagtgatgaa ctgttaggtt ctgatgactc acatgatggg gagtctgaat caaatgccaa 1620
agtagctgat gtattggacg ttctaaatga ggtagatgaa tattctggtt cttcagagaa 1680
aatagactta ctggccagtg atcctcatga ggctttaata tgtaaaagtg aaagagttca 1740
ctccaaatca gtagagagta atattgaaga caaaatattt gggaaaacct atcggaagaa 1800
ggcaagcctc cccaacttaa gccatgtaac tgaaaatcta attataggag catttgttac 1860
tgagccacag ataatacaag agcgtcccct cacaaataaa ttaaagcgta aaaggagacc 1920
tacatcaggc cttcatcctg aggattttat caagaaagca gatttggcag ttcaaaagac 1980
tcctgaaatg ataaatcagg gaactaacca aacggagcag aatggtcaag tgatgaatat 2040
tactaatagt ggtcatgaga ataaaacaaa aggtgattct attcagaatg agaaaaatcc 2100
taacccaata gaatcactcg aaaaagaatc tgctttcaaa acgaaagctg aacctataag 2160
cagcagtata agcaatatgg aactcgaatt aaatatccac aattcaaaag cacctaaaaa 2220
gaataggctg aggaggaagt cttctaccag gcatattcat gcgcttgaac tagtagtcag 2280
tagaaatcta agcccaccta attgtactga attgcaaatt gatagttgtt ctagcagtga 2340
agagataaag aaaaaaaagt acaaccaaat gccagtcagg cacagcagaa acctacaact 2400
catggaaggt aaagaacctg caactggagc caagaagagt aacaagccaa atgaacagac 2460
aagtaaaaga catgacagcg atactttccc agagctgaag ttaacaaatg cacctggttc 2520
ttttactaag tgttcaaata ccagtgaact taaagaattt gtcaatccta gccttccaag 2580
agaagaaaaa gaagagaaac tagaaacagt taaagtgtct aataatgctg aagaccccaa 2640
agatctcatg ttaagtggag aaagggtttt gcaaactgaa agatctgtag agagtagcag 2700
tatttcattg gtacctggta ctgattatgg cactcaggaa agtatctcgt tactggaagt 2760
tagcactcta gggaaggcaa aaacagaacc aaataaatgt gtgagtcagt gtgcagcatt 2820
tgaaaacccc aagggactaa ttcatggttg ttccaaagat aatagaaatg acacagaagg 2880
ctttaagtat ccattgggac atgaagttaa ccacagtcgg gaaacaagca tagaaatgga 2940
agaaagtgaa cttgatgctc agtatttgca gaatacattc aaggtttcaa agcgccagtc 3000
atttgctccg ttttcaaatc caggaaatgc agaagaggaa tgtgcaacat tctctgccca 3060
ctctgggtcc ttaaagaaac aaagtccaaa agtcactttt gaatgtgaac aaaaggaaga 3120
aaatcaagga aagaatgagt ctaatatcaa gcctgtacag acagttaata tcactgcagg 3180
ctttcctgtg gttggtcaga aagataagcc agttgataat gccaaatgta gtatcaaagg 3240
aggctctagg ttttgtctat catctcagtt cagaggcaac gaaactggac tcattactcc 3300
aaataaacat ggacttttac aaaacccata tcgtatacca ccactttttc ccatcaagtc 3360
atttgttaaa actaaatgta agaaaaatct gctagaggaa aactttgagg aacattcaat 3420
gtcacctgaa agagaaatgg gaaatgagaa cattccaagt acagtgagca caattagccg 3480
taataacatt agagaaaatg tttttaaaga agccagctca agcaatatta atgaagtagg 3540
ttccagtact aatgaagtgg gctccagtat taatgaaata ggttccagtg atgaaaacat 3600
tcaagcagaa ctaggtagaa acagagggcc aaaattgaat gctatgctta gattaggggt 3660
tttgcaacct gaggtctata aacaaagtct tcctggaagt aattgtaagc atcctgaaat 3720
aaaaaagcaa gaatatgaag aagtagttca gactgttaat acagatttct ctccatatct 3780
gatttcagat aacttagaac agcctatggg aagtagtcat gcatctcagg tttgttctga 3840
gacacctgat gacctgttag atgatggtga aataaaggaa gatactagtt ttgctgaaaa 3900
tgacattaag gaaagttctg ctgtttttag caaaagcgtc cagaaaggag agcttagcag 3960
gagtcctagc cctttcaccc atacacattt ggctcagggt taccgaagag ggccaagaaa 4020
attagagtcc tcagaagaga acttatctag tgaggatgaa gagcttccct gcttccaaca 4080
cttgttattt ggtaaagtaa acaatatacc ttctcagtct actaggcata gcaccgttgc 4140
taccgagtgt ctgtctaaga acacagagga gaatttatta tcattgaaga atagcttaaa 4200
tgactgcagt aaccaggtaa tattggcaaa ggcatctcag gaacatcacc ttagtgagga 4260
aacaaaatgt tctgctagct tgttttcttc acagtgcagt gaattggaag acttgactgc 4320
aaatacaaac acccaggatc ctttcttgat tggttcttcc aaacaaatga ggcatcagtc 4380
tgaaagccag ggagttggtc tgagtgacaa ggaattggtt tcagatgatg aagaaagagg 4440
aacgggcttg gaagaaaata atcaagaaga gcaaagcatg gattcaaact taggtgaagc 4500
agcatctggg tgtgagagtg aaacaagcgt ctctgaagac tgctcagggc tatcctctca 4560
gagtgacatt ttaaccactc agcagaggga taccatgcaa cataacctga taaagctcca 4620
gcaggaaatg gctgaactag aagctgtgtt agaacagcat gggagccagc cttctaacag 4680

ctacccttcc atcataagtg actcttctgc ccttgaggac ctgcgaaatc cagaacaaag 4740
cacatcagaa aaagcagtat taacttcaca gaaaagtagt gaatacccta taagccagaa 4800
tccagaaggc ctttctgctg acaagtttga ggtgtctgca gatagttcta ccagtaaaaa 4860
taaagaacca ggagtggaaa ggtcatcccc ttctaaatgc ccatcattag atgataggtg 4920
gtacatgcac agttgctctg ggagtcttca gaatagaaac tacccatctc aagaggagct 4980
cattaaggtt gttgatgtgg aggagcaaca gctggaagag tctgggccac acgatttgac 5040
ggaaacatct tacttgccaa ggcaagatct agagggaacc ccttacctgg aatctggaat 5100
cagcctcttc tctgatgacc ctgaatctga tccttctgaa gacagagccc cagagtcagc 5160
tcgtgttggc aacataccat cttcaacctc tgcattgaaa gttccccaat tgaaagttgc 5220
agaatctgcc cagagtccag ctgctgctca tactactgat actgctgggt ataatgcaat 5280
ggaagaaagt gtgagcaggg agaagccaga attgacagct tcaacagaaa gggtcaacaa 5340
aagaatgtcc atggtggtgt ctggcctgac cccagaagaa tttatgctcg tgtacaagtt 5400
tgccagaaaa caccacatca ctttaactaa tctaattact gaagagacta ctcatgttgt 5460
tatgaaaaca gatgctgagt ttgtgtgtga acggacactg aaatattttc taggaattgc 5520
gggaggaaaa tgggtagtta gctatttctg ggtgacccag tctattaaag aaagaaaaat 5580
gctgaatgag catgatttg aagtcagagg agatgtggtc aatggaagaa accaccaagg 5640
tccaaagcga gcaagagaat cccaggacag aaagatcttc agggggctag aaatctgttg 5700
ctatgggccc ttcaccaaca tgcccacaga tcaactggaa tggatggtac agctgtgtgg 5760
tgcttctgtg gtgaaggagc tttcatcatt caccettggc acaggtgtcc acccaattgt 5820
ggttgtgcag ccagatgcct ggacagagga caatggcttc catgcaattg ggcagatgtg 5880
tgaggcacct gtggtgaccc gagagtgggt gttggacagt gtagcactct accagtgcca 5940
ggagctggac acctacctga taccccagat cccccacagc cactactgac tgcagccagc 6000
cacaggtaca gagccacagg accccaagaa tgagcttaca aagtggcctt tccaggccct 6060
gggagctcct ctcactcttc agtccttcta ctgtcctggc tactaaatat tttatgtaca 6120
tcagcctgaa aaggacttct ggctatgcaa gggtccctta aagattttct gcttgaagtc 6180
tcccttggaa atctgccatg agcacaaaat tatggtaatt tttcacctga gaagatttta 6240
aaaccattta aacgccacca attgagcaag atgctgattc attatttatc agccctattc 6300
tttctattca ggctgttgtt ggcttagggc tggaagcaca gagtggcttg gcctcaagag 6360
aatagctggt ttccctaagt ttacttctct aaaaccctgt gttcacaaag gcagagagtc 6420
agacccttca atggaaggag agtgcttggg atcgattatg tgacttaaag tcagaatagt 6480
ccttgggcag ttctcaaatg ttggagtgga acattgggga ggaaattctg aggcaggtat 6540
tagaaatgaa aaggaaactt gaaacctggg catggtggct cacgcctgta atcccagcac 6600
tttgggaggc caaggtgggc agatcactgg aggtcaggag ttcgaaacca gcctggccaa 6660
catggtgaaa ccccatctct actaaaaata cagaaattag ccggtcatgg tggtggacac 6720
ctgtaatccc agctactcag gtggctaagg caggagaatc acttcagccc gggaggtgga 6780
ggttgcagtg agccaagatc ataccacggc actccagcct gggtgacagt gagactgtgg 6840
ctcaaaaaaa aaaaaaaaaa aggaaaatga aactaggaaa ggtttcttaa agtctgagat 6900
atatttgcta gatttctaaa gaatgtgttc taaaacagca gaagattttc aagaaccggt 6960
ttccaaagac agtcttctaa ttcctcatta gtaataagta aaatgtttat tgttgtagct 7020
ctggtatata atccattcct cttaaaatat aagacctctg gcatgaatat ttcatatcta 7080
taaaatgaca gatcccacca ggaaggaagc tgttgctttc tttgaggtga tttttttcct 7140
ttgctccctg ttgctgaaac catacagctt cataaataat tttgcttgct gaaggaagaa 7200
aaagtgtttt tcataaaccc attatccagg actgtttata gctgttggaa ggactaggtc 7260
ttccctagcc cccccagtgt gcaagggcag tgaagacttg attgtacaaa atacgttttg 7320
taaatgttgt gctgttaaca ctgcaaataa acttggtagc aaaca 7365

<210> 342
<211> 10386
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (0)...(0)
<223> n = a, t, c or g

<400> 342
attgaggact cggaaatgag gtccaagggt agccaaggat ggctgcagct tcatatgatc 60
agttgttaaa gcaagttgag gcactgaaga tggagaactc aaatcttcga caagagctag 120
aagataattc caatcatctt acaaaactgg aaactgaggc atctaatatg aaggaagtac 180
ttaaacaact acaaggaagt attgaagatg aagctatggc ttcttctgga cagattgatt 240
tattagagcg tcttaaagag cttaacttag atagcagtaa tttccctgga gtaaaactgc 300
ggtcaaaaat gtccctccgt tcttatggaa gccgggaagg atctgtatca agccgttctg 360
gagagtgcag tcctgttcct atgggttcat ttccaagaag agggtttgta aatggaagca 420
gagaaagtac tggatattta gaagaacttg agaaagagag gtcattgctt cttgctgatc 480
ttgacaaaga agaaaaggaa aaagactggt attacgctca acttcagaat ctcactaaaa 540

gaatagatag tcttccttta actgaaaatt tttccttaca aacagatatg accagaaggc 600
aattggaata tgaagcaagg caaatcagag ttgcgatgga agaacaacta ggtacctgcc 660
aggatatgga aaaacgagca cagcgaagaa tagccagaat tcagcaaatc gaaaaggaca 720
tacttcgtat acgacagctt ttacagtccc aagcaacaga agcagagagg tcatctcaga 780
acaagcatga aaccggctca catgatgctg agcggcagaa tgaaggtcaa ggagtgggag 840
aaatcaacat ggcaacttct ggtaatggtc agggttcaac tacacgaatg gaccatgaaa 900
cagccagtgt tttgagttct agtagcacac actctgcacc tcgaaggctg acaagtcatc 960
tgggaaccaa ggtggaaatg gtgtattcat tgttgtcaat gcttggtact catgataagg 1020
atgatatgtc gcgaactttg ctagctatgt ctagctccca agacagctgt atatccatgc 1080
gacagtctgg atgtcttcct ctcctcatcc agcttttaca tggcaatgac aaagactctg 1140
tattgttggg aaattcccgg ggcagtaaag aggctcgggc cagggccagt gcagcactcc 1200
acaacatcat tcactcacag cctgatgaca agagaggcag gcgtgaaatc cgagtccttc 1260
atcttttgga acagatacgc gcttactgtg aaacctgttg ggagtggcag gaagctcatg 1320
aaccaggcat ggaccaggac aaaaatccaa tgccagctcc tgttgaacat cagatctgtc 1380
ctgctgtgtg tgttctaatg aaactttcat ttgatgaaga gcatagacat gcaatgaatg 1440
aactaggggg actacaggcc attgcagaat tattgcaagt ggactgtgaa atgtacgggc 1500
ttactaatga ccactacagt attacactaa gacgatatgc tggaatggct ttgacaaact 1560
tgacttttgg agatgtagcc aacaaggcta cgctatgctc tatgaaaggc tgcatgagag 1620
cacttgtggc ccaactaaaa tctgaaagtg aagacttaca gcaggttatt gcaagtgttt 1680
tgaggaattt gtcttggcga gcagatgtaa atagtaaaaa gacgttgcga gaagttggaa 1740
gtgtgaaagc attgatggaa tgtgctttag aagttaaaaa ggaatcaacc ctcaaaagcg 1800
tattgagtgc cttatggaat ttgtcagcac attgcactga gaataaagct gatatatgtg 1860
ctgtagatgg tgcacttgca tttttggttg gcactcttac ttaccggagc cagacaaaca 1920
ctttagccat tattgaaagt ggaggtggga tattacggaa tgtgtccagc ttgatagcta 1980
caaatgagga ccacaggcaa atcctaagag agaacaactg tctacaaact ttattacaac 2040
acttaaaatc tcatagtttg acaatagtca gtaatgcatg tggaactttg tggaatctct 2100
cagcaagaaa tcctaaagac caggaagcat tatgggacat gggggcagtt agcatgctca 2160
agaacctcat tcattcaaag cacaaaatga ttgctatggg aagtgctgca gctttaagga 2220
atctcatggc aaataggcct gcgaagtaca aggatgccaa tattatgtct cctggctcaa 2280
gcttgccatc tcttcatgtt aggaaacaaa aagccctaga agcagaatta gatgctcagc 2340
acttatcaga aacttttgac aatatagaca atttaagtcc caaggcatct catcgtagta 2400
agcagagaca caagcaaagt ctctatggtg attatgtttt tgacaccaat cgacatgatg 2460
ataataggtc agacaatttt aatactggca acatgactgt cctttcacca tatttgaata 2520
ctacagtgtt acccagctcc tcttcatcaa gaggaagctt agatagttct cgttctgaaa 2580
aagatagaag tttggagaga gaacgcggaa ttggtctagg caactaccat ccagcaacag 2640
aaaatccagg aacttcttca aagcgaggtt tgcagatctc caccactgca gcccagattg 2700
ccaaagtcat ggaagaagtg tcagccattc atacctctca ggaagacaga agttctgggt 2760
ctaccactga attacattgt gtgacagatg agagaaatgc acttagaaga agctctgctg 2820
cccatacaca ttcaaacact tacaatttca ctaagtcgga aaattcaaat aggacatgtt 2880
ctatgcctta tgccaaatta gaatacaaga gatcttcaaa tgatagttta aatagtgtca 2940
gtagtagtga tggttatggt aaaagaggtc aaatgaaacc ctcgattgaa tcctattctg 3000
aagatgatga aagtaagttt tgcagttatg gtcaataccc agccgaccta gcccataaaa 3060
tacatagtgc aaatcatatg gatgataatg atggagaact agatacacca ataaattata 3120
gtcttaaata ttcagatgag cagttgaact ctggaaggca aagtccttca cagaatgaaa 3180
gatgggcaag acccaaacac ataatagaag atgaaataaa acaaagtgag caaagacaat 3240
caaggaatca aagtacaact tatcctgttt atactgagag cactgatgat aaacacctca 3300
agttccaacc acattttgga cagcaggaat gtgtttctcc atacaggtca cggggagcca 3360
atggttcaga aacaaatcga gtgggttcta atcatggaat taatcaaaat gtaagccagt 3420
ctttgtgtca agaagatgac tatgaagatg ataagcctac caattatagt gaacgttact 3480
ctgaagaaga acagcatgaa gaagaagaga gaccaacaaa ttatagcata aaatataatg 3540
aagagaaacg tcatgtggat cagcctattg attatagttt aaaatatgcc acagatattc 3600
cttcatcaca gaaacagtca ttttcattct caaagagttc atctggacaa agcagtaaaa 3660
ccgaacatat gtcttcaagc agtgagaata cgtccacacc ttcatctaat gccaagaggc 3720
agaatcagct ccatccaagt tctgcacaga gtagaagtgg tcagcctcaa aaggctgcca 3780
cttgcaaagt ttcttctatt aaccaagaaa caatacagac ttattgtgta gaagatactc 3840
caatatgttt ttcaagatgt agttcattat catctttgtc atcagctgaa gatgaaatag 3900
gatgtaatca gacgacacag gaagcagatt ctgctaatac cctgcaaata gcagaaataa 3960
aagaaaagat tggaactagg tcagctgaag atcctgtgag cgaagttcca gcagtgtcac 4020
agcaccctag aaccaaatcc agcagactgc agggttctag tttatcttca gaatcagcca 4080
ggcacaaagc tgttgaattt tcttcaggag cgaaatctcc ctccaaaagt ggtgctcaga 4140
cacccaaaag tccacctgaa cactatgttc aggagacccc actcatgttt agcagatgta 4200
cttctgtcag ttcacttgat agttttgaga gtcgttcgat tgccagctcc gttcagagtg 4260
aaccatgcag tggaatggta agtggcatta taagccccag tgatcttcca gatagccctg 4320
gacaaaccat gccaccaagc agaagtaaaa cacctccacc acctcctcaa acagctcaaa 4380
ccaagcgaga agtacctaaa aataaagcac ctactgctga aaagagagag agtggaccta 4440
agcaagctgc agtaaatgct gcagttcaga gggtccaggt tcttccagat gctgatactt 4500
tattacattt tgccacggaa agtactccag atggattttc ttgttcatcc agcctgagtg 4560
ctctgagcct cgatgagcca tttatacaga aagatgtgga attaagaata atgcctccag 4620

```
ttcaggaaaa tgacaatggg aatgaaacag aatcagagca gcctaaagaa tcaaatgaaa 4680
accaagagaa agaggcagaa aaaactattg attctgaaaa ggacctatta gatgattcag 4740
atgatgatga tattgaaata ctagaagaat gtattatttc tgccatgcca acaaagtcat 4800
cacgtaaagc aaaaaagcca gcccagactg cttcaaaatt acctccacct gtggcaagga 4860
aaccaagtca gctgcctgtg tacaaacttc taccatcaca aaacaggttg caaccccaaa 4920
agcatgttag ttttacaccg ggggatgata tgccacgggt gtattgtgtt gaagggacac 4980
ctataaactt ttccacagct acatctctaa gtgatctaac aatcgaatcc cctccaaatg 5040
agttagctgc tggagaagga gttagaggag gagcacagtc aggtgaattt gaaaaacgag 5100
ataccattcc tacagaaggc agaagtacag atgaggctca aggaggaaaa acctcatctg 5160
taaccatacc tgaattggat gacaataaag cagaggaagg tgatattctt gcagaatgca 5220
ttaattctgc tatgcccaaa gggaaaagtc acaagccttt ccgtgtgaaa aagataatgg 5280
accaggtcca gcaagcatct gcgtcgtctt ctgcacccaa caaaaatcag ttagatggta 5340
agaaaaagaa accaacttca ccagtaaaac ctataccaca aaatactgaa tataggacac 5400
gtgtaagaaa aaatgcagac tcaaaaaata atttaaatgc tgagagagtt ttctcagaca 5460
acaaagattc aaagaaacag aatttgaaaa ataattccaa ggacttcaat gataagctcc 5520
caaataatga agatagagtc agaggaagtt ttgcttttga ttcacctcat cattacacgc 5580
ctattgaagg aactccttac tgtttttcac gaaatgattc tttgagttct ctagattttg 5640
atgatgatga tgttgacctt tccagggaaa aggctgaatt aagaaaggca aaagaaaata 5700
aggaatcaga ggctaaagtt accagccaca cagaactaac ctccaaccaa caatcagcta 5760
ataagacaca agctattgca aagcagccaa taaatcgagg tcagcctaaa cccatacttc 5820
agaaacaatc cacttttccc cagtcatcca aagacatacc agacagaggg gcagcaactg 5880
atgaaaagtt acagaatttt gctattgaaa atactccagt ttgcttttct cataattcct 5940
ctctgagttc tctcagtgac attgaccaag aaaacaacaa taaagaaaat gaacctatca 6000
aagagactga gccccctgac tcacagggag aaccaagtaa acctcaagca tcaggctatg 6060
ctcctaaatc atttcatgtt gaagataccc cagtttgttt ctcaagaaac agttctctca 6120
gttctcttag tattgactct gaagatgacc tgttgcagga atgtataagc tccgcaatgc 6180
caaaaaagaa aaagccttca agactcaagg gtgataatga aaaacatagt cccagaaata 6240
tgggtggcat attaggtgaa gatctgacac ttgatttgaa agatatacag agaccagatt 6300
cagaacatgg tctatcccct gattcagaaa attttgattg gaaagctatt caggaaggtg 6360
caaattccat agtaagtagt ttacatcaag ctgctgctgc tgcatgttta tctagacaag 6420
cttcgtctga ttcagattcc atcctttccc tgaaatcagg aatctctctg ggatcaccat 6480
ttcatcttac acctgatcaa gaagaaaaac cctttacaag taataaaggc ccacgaattc 6540
taaaaccagg ggagaaaagt acattggaaa ctaaaaagat agaatctgaa agtaaaggaa 6600
tcaaaggagg aaaaaaagtt tataaaagtt tgattactgg aaaagttcga tctaattcag 6660
aaatttcagg ccaaatgaaa cagccccttc aagcaaacat gccttcaatc tctcgaggca 6720
ggacaatgat tcatattcca ggagttcgaa atagctcctc aagtacaagt cctgtttcta 6780
aaaaaggccc accccttaag actccagcct ccaaaagccc tagtgaaggt caaacagcca 6840
ccacttctcc tagaggagcc aagccatctg tgaaatcaga attaagccct gttgccaggc 6900
agacatccca aataggtggg tcaagtaaag caccttctag atcaggatct agagattcga 6960
ccccttcaag acctgcccag caaccattaa gtagacctat acagtctcct ggccgaaact 7020
caatttcccc tggtagaaat ggaataagtc ctcctaacaa attatctcaa cttccaagga 7080
catcatcccc tagtactgct tcaactaagt cctcaggttc tggaaaaatg tcatatacat 7140
ctccaggtag acagatgagc caacagaacc ttaccaaaca aacaggttta tccaagaatg 7200
ccagtagtat tccaagaagt gagtctgcct ccaaaggact aaatcagatg aataatggta 7260
atggagccaa taaaaaggta gaactttcta gaatgtcttc aactaaatca agtggaagtg 7320
aatctgatag atcagaaaga cctgtattag tacgccagtc aactttcatc aaagaagctc 7380
caagcccaac cttaagaaga aaattggagg aatctgcttc atttgaatct ctttctccat 7440
catctagacc agcttctccc actaggtccc aggcacaaac tccagtttta agtccttccc 7500
ttcctgatat gtctctatcc acacattcgt ctgttcaggc tggtggatgg cgaaaactcc 7560
cacctaatct cagtcccact atagagtata atgatggaag accagcaaag cgccatgata 7620
ttgcacggtc tcattctgaa agtccttcta gacttccaat caataggtca ggaacctgga 7680
aacgtgagca cagcaaacat tcatcatccc ttcctcgagt aagcacttgg agaagaactg 7740
gaagttcatc ttcaattctt tctgcttcat cagaatccag tgaaaaagca aaaagtgagg 7800
atgaaaaaca tgtgaactct atttcaggaa ccaaacaaag taaagaaaac caagtatccg 7860
caaaaggaac atggagaaaa ataaaagaaa atgaattttc tcccacaaat agtacttctc 7920
agaccgtttc ctcaggtgct acaaatggtg ctgaatcaaa gactctaatt tatcaaatgg 7980
cacctgctgt ttctaaaaca gaggatgttt gggtgagaat tgaggactgt cccattaaca 8040
atcctagatc tggaagatct cccacaggta atactccccc ggtgattgac agtgtttcag 8100
aaaaggcaaa tccaaacatt aaagattcaa aagataatca ggcaaaacaa aatgtgggta 8160
atggcagtgt tcccatgcgt accgtgggtt tggaaaatcg cctgaactcc tttattcagg 8220
tggatgcccc tgaccaaaaa ggaactgaga taaaaccagg acaaaataat cctgtccctg 8280
tatcagagac taatgaaagt tctatagtgg aacgtacccc attcagttct agcagctcaa 8340
gcaaacacag ttcacctagt gggactgttg ctgccagagt gactcctttt aattacaacc 8400
caagccctag gaaaagcagc gcagatagca cttcagctcg gccatctcag atcccaactc 8460
cagtgaataa caacacaaag aagcgagatt ccaaaactga cagcacagaa tccagtggaa 8520
cccaaagtcc taagcgccat tctgggtctt accttgtgac atctgtttaa aagagaggaa 8580
gaatgaaact aagaaaattc tatgttaatt acaactgcta tatagacatt ttgtttcaaa 8640
tgaaacttta aaagactgaa aaattttgta aataggtttg attcttgtta gagggttttt 8700
```

gttctggaag ccatatttga tagtatactt tgtcttcact ggtcttattt tgggaggcac 8760
tcttgatggt taggaaaaaa atagtaaagc caagtatgtt tgtacagtat gttttacatg 8820
tatttaaagt agcatcccat cccaacttcc tttaattatt gcttgtctta aaataatgaa 8880
cactacagat agaaaatatg atatattgct gttatcaatc atttctagat tataaactga 8940
ctaaacttac atcagggaaa aattggtatt tatgcaaaaa aaaatgtttt tgtccttgtg 9000
agtccatcta acatcataat taatcatgtg gctgtgaaat tcacagtaat atggttcccg 9060
atgaacaagc tttacccagc ctgtttgctt tactgcatga atgaaactga tggttcaatt 9120
tcagaagtaa tgattaacag ttatgtggtc acatgatgtg catagagata gctacagtgt 9180
aataatttac actattttgt gctccaaaca aaacaaaaat ctgtgtaact gtaaaacatt 9240
gaatgaaact attttacctg aactagattt tatctgaaag taggtagaat ttttgctatg 9300
ctgtaatttg ttgtatattc tggtatttga ggtgagatgg ctgctctttt attaatgaga 9360
catgaattgt gtctcaacag aaactaaatg aacatttcag aataaattat tgctgtatgt 9420
aaactgttac tgaaattggt atttgtttga agggtcttgt ttcacatttg tattaataat 9480
tgtttaaaat gcctctttta aaagcttata taaatttttt ncttcagctt ctatgcatta 9540
agagtaaaat tcctcttact gtaataaaaa caattgaaga agactgttgc cacttaacca 9600
ttccatgcgt tggcacttat ctattcctga aattctttta tgtgattagc tcatcttgat 9660
ttttaacatt tttccactta aacttttttt tcttactcca ctggagctca gtaaaagtaa 9720
attcatgtaa tagcaatgca agcagcctag cacagactaa gcattgagca taataggccc 9780
acataatttc ctctttctta atattataga aattctgtac ttgaaattga ttcttagaca 9840
ttgcagtctc ttcgaggctt tacagtgtaa actgtcttgc cccttcatct tcttgttgca 9900
actgggtctg acatgaacac tttttatcac cctgtatgtt agggcaagat ctcagcagtg 9960
aagtataatc agcactttgc catgctcaga aaattcaaat cacatggaac tttagaggta 10020
gatttaatac gattaagata ttcagaagta tattttagaa tccctgcctg ttaaggaaac 10080
tttatttgtg gtaggtacag ttctggggta catgttaagt gtccccttat acagtggagg 10140
gaagtcttcc ttcctgaagg aaaataaact gacacttatt aactaagata atttacttaa 10200
tatatcttcc ctgatttgtt ttaaaagatc agagggtgac tgatgataca tgcatacata 10260
tttgttgaat aaatgaaaat ttatttttag tgataagatt catacactct gtatttgggg 10320
agagaaaacc tttttaagca tggtggggca ctcagatagg agtgaataca cctacctggt 10380
ggtcat 10386

<210> 343
<211> 2191
<212> DNA
<213> Homo sapiens

<400> 343
ggtggccgag cgggggaccg ggaagcatgg cccgggggtc ggcggttgcc tgggcggcgc 60
tcgggccgtt gttgtggggc tgcgcgctgg ggctgcaggg cgggatgctg tacccccagg 120
agagcccgtc gcgggagtgc aaggagctgg acggcctctg gagcttccgc gccgacttct 180
ctgacaaccg acgccggggc ttcgaggagc agtggtaccg gcggccgctg tgggagtcag 240
gccccaccgt ggacatgcca gttccctcca gcttcaatga catcagccag gactggcgtc 300
tgcggcattt tgtcggctgg gtgtggtacg aacgggaggt gatcctgccg gagcgatgga 360
cccaggacct gcgcacaaga gtggtgctga ggattggcag tgcccattcc tatgccatcg 420
tgtgggtgaa tggggtcgac acgctagagc atgagggggg ctacctcccc ttcgaggccg 480
acatcagcaa cctggtccag gtggggcccc tgccctcccg gctccgaatc actatcgcca 540
tcaacaacac actcaccccc accaccctgc caccagggac catccaatac ctgactgaca 600
cctccaagta tcccaagggt tactttgtcc agaacacata ttttgacttt ttcaactacg 660
ctggactgca gcggtctgta cttctgtaca cgacacccac cacctacatc gatgacatca 720
ccgtcaccac cagcgtggag caagacagtg ggctggtgaa ttaccagatc tctgtcaagg 780
gcagtaacct gttcaagttg gaagtgcgtc ttttggatgc agaaaacaaa gtcgtggcga 840
atgggactgg gacccagggc caacttaagg tgccaggtgt cagcctctgg tggccgtacc 900
tgatgcacga acgccctgcc tatctgtatt cattggaggt gcagctgact gcacagacgt 960
cactggggcc tgtgtctgac ttctacacac tccctgtggg gatccgcact gtggctgtca 1020
ccaagagcca gttcctcatc aatgggaaac ctttctattt ccacggtgtc aacaagcatg 1080
aggatgcgga catccgaggg aagggcttcg actggccgct gctggtgaag gacttcaacc 1140
tgcttcgctg gcttggtgcc aacgctttcc gtaccagcca ctacccctat gcagaggaag 1200
tgatgcagat gtgtgaccgc tatgggattg tggtcatcga tgagtgtccc ggcgtgggcc 1260
tggcgctgcc gcagttcttc aacaacgttt ctctgcatca ccacatgcag gtgatggaag 1320
aagtggtgcg tagggacaag aaccaccccg cggtcgtgat gtggtctgtg gccaacgagc 1380
ctgcgtccca cctagaatct gctggctact acttgaagat ggtgatcgct cacaccaaat 1440
ccttggaccc ctcccggcct gtgacctttg tgagcaactc taactatgca gcagacaagg 1500
gggctccgta tgtggatgtg atctgtttga acagctacta ctcttggtat cacgactacg 1560
ggcacctgga gttgattcag ctgcagctgg ccacccagtt tgagaactgg tataagaagt 1620
atcagaagcc cattattcag agcgagtatg gagcagaaac gattgcaggg tttcaccagg 1680
atccacctct gatgttcact gaagagtacc agaaaagtct gctagagcag taccatctgg 1740
gtctggatca aaaacgcaga aaatatgtgg ttggagagct catttggaat tttgccgatt 1800

tcatgactga acagtcaccg acgagagtgc tggggaataa aaaggggatc ttcactcggc 1860
agagacaacc aaaaagtgca gcgttccttt tgcgagagag atactggaag attgccaatg 1920
aaaccaggta tccccactca gtagccaagt cacaatgttt ggaaaacagc ccgtttactt 1980
gagcaagact gataccacct gcgtgtccct tcctccccga gtcagggcga cttccacagc 2040
agcagaacaa gtgcctcctg gactgttcac ggcagaccag aacgtttctg gcctgggttt 2100
tgtggtcatc tattctagca gggaacacta aaggtggaaa taaaagattt tctattatgg 2160
aaataaagag ttggcatgaa agtcgctact g 2191

<210> 344
<211> 2776
<212> DNA
<213> Homo sapiens

<400> 344
cagggcagac tggtagcaaa gcccccacgc ccagccagga gcaccgccgc ggactccagc 60
acaccgaggg acatgctggg cctgcgcccc ccactgctcg ccctggtggg gctgctctcc 120
ctcgggtgcg tcctctctca ggagtgcacg aagttcaagg tcagcagctg ccgggaatgc 180
atcgagtcgg ggcccggctg cacctggtgc cagaagctga acttcacagg gccgggggat 240
cctgactcca ttcgctgcga cacccggcca cagctgctca tgaggggctg tgcggctgac 300
gacatcatgg accccacaag cctcgctgaa acccaggaag accacaatgg gggccagaag 360
cagctgtccc cacaaaaagt gacgctttac ctgcgaccag gccaggcagc agcgttcaac 420
gtgaccttcc ggcgggccaa gggctacccc atcgacctgt actatctgat ggacctctcc 480
tactccatgc ttgatgacct caggaatgtc aagaagctag gtggcgacct gctccgggcc 540
ctcaacgaga tcaccgagtc cggccgcatt ggcttcgggt ccttcgtgga caagaccgtg 600
ctgccgttcg tgaacacgca ccctgataag ctgcgaaacc catgccccaa caaggagaaa 660
gagtgccagc cccgtttgc cttcaggcac gtgctgaagc tgaccaacaa ctccaaccag 720
tttcagaccg aggtcgggaa gcagctgatt tccggaaacc tggatgcacc cgagggtggg 780
ctggacgcca tgatgcaggt cgccgcctgc ccggaggaaa tcggctggcg caacgtcacg 840
cggctgctgg tgtttgccac tgatgacggc ttccatttcg cgggcgacgg aaagctgggc 900
gccatcctga cccccaacga cggccgctgt cacctggagg acaacttgta caagaggagc 960
aacgaattcg actacccatc ggtgggccag ctggcgcaca agctggctga aaacaacatc 1020
cagcccatct tcgcggtgac cagtaggatg gtgaagacct acgagaaact caccgagatc 1080
atccccaagt cagccgtggg ggagctgtct gaggactcca gcaatgtggt ccatctcatt 1140
aagaatgctt acaataaact ctcctccagg gtcttcctgg atcacaacgc cctccccgac 1200
accctgaaag tcacctacga ctccttctgc agcaatggag tgacgcacag gaaccagccc 1260
agaggtgact gtgatggcgt gcagatcaat gtcccgatca ccttccaggt gaaggtcacg 1320
gccacagagt gcatccagga gcagtcgttt gtcatccggg cgctgggctt cacggacata 1380
gtgaccgtgc aggttcttcc ccagtgtgag tgccggtgcc gggaccagag cagagaccgc 1440
agcctctgcc atggcaaggg cttcttggag tgcggcatct gcaggtgtga cactggctac 1500
attgggaaaa actgtgagtg ccagacacag ggccggagca gccaggagct ggaaggaagc 1560
tgccggaagg acaacaactc catcatctgc tcagggctgg gggactgtgt ctgcgggcag 1620
tgcctgtgcc acaccagcga cgtccccggc aagctgatat acgggcagta ctgcgagtgt 1680
gacaccatca actgtgagcg ctacaacggc caggtctgcg gcggcccggg gagggggctc 1740
tgcttctgcg ggaagtgccg ctgccacccg ggctttgagg gctcagcgtg ccagtgcgag 1800
aggaccactg agggctgcct gaacccgcgg cgtgttgagt gtagtggtcg tggccggtgc 1860
cgctgcaacg tatgcgagtg ccattcaggc taccagctgc ctctgtgcca ggagtgcccc 1920
ggctgcccct caccctgtgg caagtacatc tcctgcgccg agtgcctgaa gttcgaaaag 1980
ggcccctttg ggaagaactg cagcgcggcg tgtccgggcc tgcagctgtc gaacaacccc 2040
gtgaagggca ggacctgcaa ggagagggac tcagagggct gctgggtggc ctacacgctg 2100
gagcagcagg acgggatgga ccgctacctc atctatgtgg atgagagccg agagtgtgtg 2160
gcaggcccca acatcgccgc catcgtcggg ggcaccgtgg caggcatcgt gctgatcggc 2220
attctcctgc tggtcatctg gaaggctctg atccacctga gcgacctccg ggagtacagg 2280
cgctttgaga aggagaagct caagtcccag tggaacaatg ataatcccct tttcaagagc 2340
gccaccacga cggtcatgaa ccccaagttt gctgagagtt aggagcactt ggtgaagaca 2400
aggccgtcag gacccaccat gtctgcccca tcacgcggcc gagacatggc ttggccacag 2460
ctcttgagga tgtcaccaat taaccagaaa tccagttatt ttccgccctc aaaatgacag 2520
ccatggccgg ccggtgcttc tgggggctcg tcggggggac agctccactc tgactggcac 2580
agtctttgca tggagacttg aggagggctt gaggttggtg aggttaggtg cgtgtttcct 2640
gtgcaagtca ggacatcagt ctgattaaag gtggtgccaa tttatttaca tttaaacttg 2700
tcagggtata aaatgacatc ccattaatta tattgttaat caatcacgtg tatagaaaaa 2760
aaaataaaac ttcaat 2776

<210> 345
<211> 3160
<212> DNA
<213> Homo sapiens

<400> 345

cctcccctcg cccggcgcgg tcccgtccgc ctctcgctcg cctcccgcct cccctcggtc 60
ttccgaggcg cccgggctcc cggcgcggcg gcggaggggg cgggcaggcc ggcgggcggt 120
gatgtggcag gactctttat gcgctgcggc aggatacgcg ctcggcgctg ggacgcgact 180
gcgctcagtt ctctcctctc ggaagctgca gccatgatgg aagtttgaga gttgagccgc 240
tgtgaggcga ggccgggctc aggcgaggga gatgagagac ggcggcggcc gcggcccgga 300
gcccctctca gcgcctgtga gcagccgcgg gggcagcgcc ctcggggagc cggccggcct 360
gcggcggcgg cagcggcggc gtttctcgcc tcctcttcgt cttttctaac cgtgcagcct 420
cttcctcggc ttctcctgaa agggaaggtg gaagccgtgg gctcgggcgg gagccggctg 480
aggcgcggcg gcggcggcgg cggcacctcc cgctcctgga gcggggggga gaagcggcgg 540
cggcggcggc cgcggcggct gcagctccag ggagggggtc tgagtcgcct gtcaccattt 600
ccagggctgg gaacgccgga gagttggtct ctccccttct actgcctcca acacggcggc 660
ggcggcggcg gcacatccag ggacccgggc cggttttaaa cctcccgtcc gccgccgccg 720
caccccccgt ggcccgggct ccggaggccg ccggcggagg cagccgttcg gaggattatt 780
cgtcttctcc ccattccgct gccgccgctg ccaggcctct ggctgctgag gagaagcagg 840
cccagtcgct gcaaccatcc agcagccgcc gcagcagcca ttacccggct gcggtccaga 900
gccaagcggc ggcagagcga ggggcatcag ctaccgccaa gtccagagcc atttccatcc 960
tgcagaagaa gccccgccac cagcagcttc tgccatctct ctcctccttt ttcttcagcc 1020
acaggctccc agacatgaca gccatcatca aagagatcgt tagcagaaac aaaaggagat 1080
atcaagagga tggattcgac ttagacttga cctatattta tccaaacatt attgctatgg 1140
gatttcctgc agaaagactt gaaggcgtat acaggaacaa tattgatgat gtagtaaggt 1200
ttttggattc aaagcataaa aaccattaca agatatacaa tctttgtgct gaaagacatt 1260
atgacaccgc caaatttaat tgcagagttg cacaatatcc ttttgaagac cataacccac 1320
cacagctaga acttatcaaa cccttttgtg aagatcttga ccaatggcta agtgaagatg 1380
acaatcatgt tgcagcaatt cactgtaaag ctggaaaggg acgaactggt gtaatgatat 1440
gtgcatattt attacatcgg ggcaaatttt taaaggcaca agaggcccta gatttctatg 1500
gggaagtaag gaccagagac aaaaagggag taactattcc cagtcagagg cgctatgtgt 1560
attattatag ctacctgtta aagaatcatc tggattatag accagtggca ctgttgtttc 1620
acaagatgat gtttgaaact attccaatgt tcagtggcgg aacttgcaat cctcagtttg 1680
tggtctgcca gctaaaggtg aagatatatt cctccaattc aggacccaca cgacgggaag 1740
acaagttcat gtactttgag ttccctcagc cgttacctgt gtgtggtgat atcaaagtag 1800
agttcttcca caaacagaac aagatgctaa aaaaggacaa aatgtttcac ttttgggtaa 1860
atacattctt cataccagga ccagaggaaa cctcagaaaa agtagaaaat ggaagtctat 1920
gtgatcaaga aatcgatagc atttgcagta tagagcgtgc agataatgac aaggaatatc 1980
tagtacttac tttaacaaaa aatgatcttg acaaagcaaa taaagacaaa gccaaccgat 2040
acttttctcc aaattttaag gtgaagctgt acttcacaaa aacagtagag gagccgtcaa 2100
atccagaggc tagcagttca acttctgtaa caccagatgt tagtgacaat gaacctgatc 2160
attatagata ttctgacacc actgactctg atccagagaa tgaacctttt gatgaagatc 2220
agcatacaca aattacaaaa gtctgaattt ttttttatca agagggataa aacaccatga 2280
aaataaactt gaataaactg aaaatggacc ttttttttt taatggcaat aggacattgt 2340
gtcagattac cagttatagg aacaattctc ttttcctgac caatcttgtt ttaccctata 2400
catccacagg gttttgacac ttgttgtcca gttgaaaaaa ggttgtgtag ctgtgtcatg 2460
tatatacctt tttgtgtcaa aaggacattt aaaattcaat taggattaat aaagatggca 2520
ctttcccgtt ttattccagt tttataaaaa gtggagacag actgatgtgt atacgtagga 2580
attttttcct tttgtgttct gtcaccaact gaagtggcta aagagctttg tgatatactg 2640
gttcacatcc tacccctttg cacttgtggc aacagataag tttgcagttg gctaagagag 2700
gtttccgaaa ggttttgcta ccattctaat gcatgtattc gggttagggc aatggagggg 2760
aatgctcaga aaggaaataa ttttatgctg gactctggac catataccat ctccagctat 2820
ttacacacac ctttctttag catgctacag ttattaatct ggacattcga ggaattggcc 2880
gctgtcactg cttgttgttt gcgcattttt ttttaaagca tattggtgct agaaaaggca 2940
gctaaaggaa gtgaatctgt attggggtac aggaatgaac cttctgcaac atcttaagat 3000
ccacaaatga agggatataa aaataatgtc ataggtaaga aacacagcaa caatgactta 3060
accatataaa tgtggaggct atcaacaaag aatgggcttg aaacattata aaaattgaca 3120
atgatttatt aaatatgttt tctcaattgt aaaaaaaaaa 3160

<210> 346
<211> 2629
<212> DNA
<213> Homo sapiens

<400> 346
acttgtcatg gcgactgtcc agctttgtgc caggagcctc gcaggggttg atgggattgg 60
ggttttcccc tcccatgtgc tcaagactgg cgctaaaagt tttgagcttc tcaaaagtct 120
agagccaccg tccagggagc aggtagctgc tgggctccgg ggacactttg cgttcgggct 180
gggagcgtgc tttccacgac ggtgacacgc ttccctggat tggcagccag actgccttcc 240
gggtcactgc catggaggag ccgcagtcag atcctagcgt cgagcccccct ctgagtcagg 300
aaacattttc agacctatgg aaactacttc ctgaaaacaa cgttctgtcc cccttgccgt 360
cccaagcaat ggatgatttg atgctgtccc cggacgatat tgaacaatgg ttcactgaag 420
acccaggtcc agatgaagct cccagaatgc cagaggctgc tccccgcgtg gcccctgcac 480

cagcagctcc tacaccggcg gcccctgcac cagccccctc ctggcccctg tcatcttctg 540
tcccttccca gaaaacctac cagggcagct acggtttccg tctgggcttc ttgcattctg 600
ggacagccaa gtctgtgact tgcacgtact cccctgccct caacaagatg ttttgccaac 660
tggccaagac ctgccctgtg cagctgtggg ttgattccac acccccgccc ggcacccgcg 720
tccgcgccat ggccatctac aagcagtcac agcacatgac ggaggttgtg aggcgctgcc 780
cccaccatga gcgctgctca gatagcgatg gtctggcccc tcctcagcat cttatccgag 840
tggaaggaaa tttgcgtgtg gagtatttgg atgacagaaa cacttttcga catagtgtgg 900
tggtgcccta tgagccgcct gaggttggct ctgactgtac caccatccac tacaactaca 960
tgtgtaacag ttcctgcatg ggcggcatga accggaggcc catcctcacc atcatcacac 1020
tggaagactc cagtggtaat ctactgggac ggaacagctt tgaggtgcgt gtttgtgcct 1080
gtcctgggag agaccggcgc acagaggaag agaatctccg caagaaaggg gagcctcacc 1140
acgagctgcc cccagggagc actaagcgag cactgcccaa caacaccagc tcctctcccc 1200
agccaaagaa gaaaccactg gatggagaat atttcaccct tcagatccgt gggcgtgagc 1260
gcttcgagat gttccgagag ctgaatgagg ccttggaact caaggatgcc caggctggga 1320
aggagccagg ggggagcagg gctcactcca gccacctgaa gtccaaaaag ggtcagtcta 1380
cctcccgcca taaaaaactc atgttcaaga cagaagggcc tgactcagac tgacattctc 1440
cacttcttgt tccccactga cagcctccca cccccatctc tccctcccct gccattttgg 1500
gttttgggtc tttgaaccct tgcttgcaat aggtgtgcgt cagaagcacc caggacttcc 1560
atttgctttg tcccggggct ccactgaaca agttggcctg cactggtgtt ttgttgtggg 1620
gaggaggatg gggagtagga catacccagct tagattttaa ggtttttact gtgagggatg 1680
tttgggagat gtaagaaatg ttcttgcagt taagggttag tttacaatca gccacattct 1740
aggtaggtag gggcccactt caccgtacta accagggaag ctgtccctca tgttgaattt 1800
tctctaactt caaggcccat atctgtgaaa tgctggcatt tgcacctacc tcacagagtg 1860
cattgtgagg gttaatgaaa taatgtacat ctggccttga aaccaccttt tattacatgg 1920
ggtctaaaac ttgacccccct tgagggtgcc tgttccctct ccctctccct gttggctggt 1980
gggttggtag tttctacagt tgggcagctg gttaggtaga gggagttgtc aagtcttgct 2040
ggcccagcca aaccctgtct gacaacctct tggtcgacct tagtacctaa aaggaaatct 2100
caccccatcc cacaccctgg aggatttcat ctcttgtata tgatgatctg gatccaccaa 2160
gacttgtttt atgctcaggg tcaatttctt ttttcttttt tttttttttt tttctttttc 2220
tttgagactg ggtctcgctt tgttgcccag gctggagtgg agtggcgtga tcttggctta 2280
ctgcagcctt tgcctccccg gctcgagcag tcctgcctca gcctccggag tagctgggac 2340
cacaggttca tgccaccatg gccagccaac ttttgcatgt tttgtagaga tggggtctca 2400
cagtgttgcc caggctggtc tcaaactcct gggctcaggc gatccacctg tctcagcctc 2460
ccagagtgct gggattacaa ttgtgagcca ccacgtggag ctggaagggt caacatcttt 2520
tacattctgc aagcacatct gcattttcac ccccaccttc ccctccttct ccctttttat 2580
atcccatttt tatatcgatc tcttatttta caataaaact ttgctgcca 2629

<210> 347
<211> 3442
<212> DNA
<213> Homo sapiens

<400> 347
agccggtgcg ccgcagacta gggcgcctcg ggccagggag cgcggaggag ccatggccac 60
cgctaacggg gccgtggaaa acgggcagcc ggacgggaag ccgccggccc tgccgcgccc 120
catccgcaac ctggaggtca agttcaccaa gatatttatc aacaatgaat ggcacgaatc 180
caagagtggg aaaaagtttg ctacatgtaa cccttcaact cgggagcaaa tatgtgaagt 240
ggaagaagga gataagcccg acgtggacaa ggctgtggag gctgcacagg ttgccttcca 300
gaggggctcg ccatggcgcc ggctggatgc cctgagtcgt gggcggctgc tgcaccagct 360
ggctgacctg gtggagaggg accgcgccac cttggccgcc ctggagacga tggatacagg 420
gaagccattt cttcatgctt ttttcatcga cctggagggc tgtattagaa ccctcagata 480
ctttgcaggg tgggcagaca aaatccaggg caagaccatc cccacagatg acaacgtcgt 540
atgcttcacc aggcatgagc ccattggtgt ctgtggggcc atcactccat ggaacttccc 600
cctgctgatg ctggtgtgga agctggcacc cgccctctgc tgtgggaaca ccatggtcct 660
gaagcctgcg gagcagacac ctctcaccgc cctttatctc ggctctctga tcaaagaggc 720
cgggttccct ccaggagtgg tgaacattgt gccaggattc gggcccacag tgggagcagc 780
aatttcttct caccctcaga tcaacaagat cgccttcacc ggctccacag aggttggaaa 840
actggttaaa gaagctgcgt cccggagcaa tctgaagcgg gtgacgctgg agctgggggg 900
gaagaacccc tgcatcgtgt gtgcggacgc tgacttggac ttggcagtgg agtgtgccca 960
tcagggagtg ttcttcaacc aaggccagtg ttgcacggca gcctccaggg tgttcgtgga 1020
ggagcaggtc tactctgagt ttgtcaggcg gagcgtggag tatgccaaga aacggcccgt 1080
gggagacccc ttcgatgtca aaacagaaca ggggcctcag attgatcaaa agcagttcga 1140
caaaatctta gagctgatcg agagtgggaa gaaggaaggg gccaagctgg aatgcggggg 1200
ctcagccatg gaagacaagg ggctcttcat caaacccact gtcttctcag aagtcacaga 1260
caacatgcgg attgccaaag aggagatttt cggccagtg caaccaatac tgaagttcaa 1320
aagtatcgaa gaagtgataa aaagagcgaa tagcaccgac tatggactca cagcagccgt 1380
gttcacaaaa aatctcgaca aagccctgaa gttggcttct gccttagagt ctggaacggt 1440
ctggatcaac tgctacaacg ccctctatgc acaggctcca tttggtggct ttaaaatgtc 1500

aggaaatggc agagaactag gtgaatacgc tttggccgaa tacacagaag tgaaaactgt 1560
caccatcaaa cttggcgaca agaacccctg aaggaaaggc ggggctcctt cctcaaacat 1620
cggacggcgg aatgtggcag atgaaatgtg ctggaggaaa aaaatgacat ttctgacctt 1680
cccgggacac attcttctgg aggctttaca tctactggag ttgaatgatt gctgttttcc 1740
tctcactctc ctgtttattc accagactgg ggatgcctat aggttgtctg tgaaatcgca 1800
gtcctgcctg gggagggagc tgttggccat ttctgtgttt cccctttaaac cagatcctgg 1860
agacagtgag atactcaggg cgttgttaac agggagtggt atttgaagtg tccagcagtt 1920
gcttgaaatg ctttgccgaa tctgactcca gtaagaatgt gggaaaaccc cctgtgtgtt 1980
ctgcaagcag ggctcttgca ccagcggtct cctcagggtg gacctgctta cagagcaagc 2040
cacgcctctt tccgaggtga aggtgggacc attccttggg aaaggattca cagtaaggtt 2100
ttttggtttt tgttttttgt tttcttgttt ttaaaaaaag gatttcacag tgagaaagtt 2160
ttggttagtg cataccgtgg aagggcgcca gggtctttgt ggattgcatg ttgacattga 2220
ccgtgagatt cggcttcaaa ccaatactgc ctttggaata tgacagaatc aatagcccag 2280
agagcttagt caaagacgat atcacggtct accttaacca aggcactttc ttaagcagaa 2340
aatattgttg aggttacctt tgctgctaaa gatccaatct tctaacgcca caacagcata 2400
gcaaatccta ggataattca cctcctcatt tgacaaatca gagctgtaat tcactttaac 2460
aaattacgca tttctatcac gttcactaac agcttatgat aagtctgtgt agtcttcctt 2520
ttctccagtt ctgttaccca atttagatta gtaaagcgta cacaactgga aagactgctg 2580
taataacaca gccttgttat ttttaagtcc tattttgata ttaatttctg attagttagt 2640
aaataacacc tggattctat ggaggacctc ggtcttcatc caagtggcct gagtatttca 2700
ctggcaggtt gtgaattttt cttttcctct ttgggaatcc aaatgatgat gtgcaatttc 2760
atgttttaac ttgggaaact gaaagtgttc ccatatagct tcaaaaacaa aaacaaatgt 2820
gttatccgac ggatactttt atggttacta actagtactt tcctaattgg gaaagtagtg 2880
cttaagtttg caaattaagt tggggagggc aataataaaa tgagggcccg taacagaacc 2940
agtgtgtgta taacgaaaac catgtataaa atgggcctat caccccttgtc agagatataa 3000
attaccacat ttggcttccc ttcatcagct aacacttatc acttatacta ccaataactt 3060
gttaaatcag gatttggctt catacactga attttcagta ttttatctca agtagatata 3120
gacactaacc ttgatagtga tacgttagag ggttcctatt cttccattgt acgataatgt 3180
ctttaatatg aaatgctaca ttatttataa ttggtagagt tattgtatct ttttatagtt 3240
gtaagtacac agaggtggta tatttaaact tctgtaatat actgtattta gaaatggaaa 3300
tatatatagt gttaggtttc acttctttta aggtttaccc ctgtggtgtg gtttaaaaat 3360
ctataggcct gggaattccg atcctagctg cagatcgcat cccacaatgc gagaatgata 3420
aaataaaatt ggatatttga ga 3442

<210> 348
<211> 737
<212> DNA
<213> Homo sapiens

<400> 348
ggagtttcgc cgccgcagtc ttcgccacca tgccgcccta caccgtggtc tatttcccag 60
ttcgaggccg ctgcgcggcc ctgcgcatgc tgctggcaga tcagggccag agctggaagg 120
aggaggtggt gaccgtggag acgtggcagg agggctcact caaagcctcc tgcctatacg 180
ggcagctccc caagttccag gacggagacc tcaccctgta ccagtccaat accatcctgc 240
gtcacctggg ccgcacccctt gggctctatg ggaaggacca gcaggaggca gccctggtgg 300
acatggtgaa tgacggcgtg gaggacctcc gctgcaaata catctccctc atctacacca 360
actatgaggc gggcaaggat gactatgtga aggcactgcc cgggcaactg aagcctttttg 420
agaccctgct gtcccagaac cagggaggca agaccttcat tgtgggagac cagatctcct 480
tcgctgacta caacctgctg gacttgctgc tgatccatga ggtcctagcc cctggctgcc 540
tggatgcgtt cccccctgctc tcagcatatg tggggcgcct cagcgcccgg cccaagctca 600
aggccttcct ggcctcccct gagtacgtga acctccccat caatggcaac gggaaacagt 660
gagggttggg gggactctga gcgggaggca gagtttgcct tcctttctcc aggaccaata 720
aaatttctaa gagagct 737

<210> 349
<211> 5189
<212> DNA
<213> Homo sapiens

<400> 349
atggccaagt cgggtggctg cggcgcggga gccggcgtgg gcggcggcaa cggggcactg 60
acctgggtga acaatgctgc aaaaaaagaa gagtcagaaa ctgccaacaa aaatgattct 120
tcaaagaagt tgtctgttga gagagtgtat cagaagaaga cacaacttga acacattctt 180
cttcgtcctg atacatatat tgggtcagtg gagccattga cgcagttcat gtgggtgtat 240
gatgaagatg taggaatgaa ttgcagggag gttacctttg tgccaggttt atacaagatc 300
tttgatgaaa ttttggttaa tgctgctgac aataaacaga gggataagaa catgacttgt 360
attaaagttt ctattgatcc tgaatctaac attataagca tttggaataa tgggaaaggc 420
attccagtag tagaacacaa ggtagagaaa gtttatgttc ctgctttaat tttggacag 480

cttttaacat ccagtaacta tgatgatgat gagaaaaaag ttacaggtgg tcgtaatggt 540
tatggtgcaa aactttgtaa tattttcagt acaaagttta cagtagaaac agcttgcaaa 600
gaatacaaac acagttttaa gcagacatgg atgaataata tgatgaagac ttctgaagcc 660
aaaattaaac attttgatgg tgaagattac acatgcataa cattccaacc agatctgtcc 720
aaatttaaga tggaaaaact tgacaaggat attgtggccc tcatgactag aagggcatat 780
gatttggctg gttcgtgtag aggggtcaag gtcatgttta atggaaagaa attgcctgta 840
aatggatttc gcagttatgt agatctttat gtgaaagaca aattggatga aactggggtg 900
gccctgaaag ttattcatga gcttgcaaat gaaagatggg atgtttgtct cacattgagt 960
gaaaaaggat tccagcaaat cagctttgta aatagtattg caactacaaa aggtggacgg 1020
cacgtggatt atgtggtaga tcaagttgtt ggtaaactga ttgaagtagt taagaaaaag 1080
aacaaagctg gtgtatcagt gaaaccattt caagtaaaaa accatatatg ggtttttatt 1140
aattgcctta ttgaaaatcc aacttttgat tctcagacta aggaaaacat gactctgcag 1200
cccaaaagtt ttgggtctaa atgccagctg tcagaaaaat tttttaaagc agcctctaat 1260
tgtggcattg tagaaagtat cctgaactgg gtgaaattta aggctcagac tcagctgaat 1320
aagaagtgtt catcagtaaa atacagtaaa atcaaaggta ttcccaaact ggatgatgct 1380
aatgatgctg gtggtaaaca ttccctggag tgtacactga tattaacaga gggagactct 1440
gccaaatcac tggctgtgtc tggattaggt gtgattggac gagacagata cggagttttt 1500
ccactcaggg gcaaaattct taatgtacgg gaagcttctc ataaacagat catggaaaat 1560
gctgaaataa ataatattat taaaatagtt ggtctacaat ataagaaaag ttacgatgat 1620
gcagaatctc tgaaaacctt acgctatgga aagattatga ttatgaccga tcaggatcaa 1680
gatggttctc acataaaagg cctgcttatt aatttcatcc atcacaattg gccatcactt 1740
ttgaagcatg gtttcttgga agagttcatt actcctattg taaaggcaag caaaaataag 1800
caggaacttt ccttctacag tattcctgaa tttgacgaat ggaaaaaaca tatagaaaac 1860
cagaaagcct ggaaaataaa gtactataaa ggattgggta ctagtacagc taaagaagca 1920
aaggaatatt ttgctgatat ggaaaggcat cgcatcttgt ttagatatgc tggtcctgaa 1980
gatgatgctg ccattacctt ggcatttagt aagaagaaga ttgatgacag aaaagaatgg 2040
ttaacaaatt ttatggaaga ccggagacag cgtaggctac atggcttacc agagcaattt 2100
ttatatggta ctgcaacaaa gcatttgact tataatgatt tcatcaacaa ggaattgatt 2160
ctcttctcaa actcagacaa tgaaagatct ataccatctc ttgttgatgg ctttaaacct 2220
ggccagcgga aagtttttatt tacctgtttc aagaggaatg ataaacgtga agtaaaagtt 2280
gcccagttgg ctggctctgt tgctgagatg tcggcttatc atcatggaga acaagcattg 2340
atgatgacta ttgtgaattt ggctcagaac tttgtgggaa gtaacaacat taacttgctt 2400
cagcctattg gtcagtttgg aactcggctt catggtggca aagatgctgc aagccctcgt 2460
tatattttca caatgttaag cactttagca aggctacttt ttcctgctgt ggatgacaac 2520
ctccttaagt tcctttatga tgataatcaa cgtgtagagc ctgagtggta tattcctata 2580
attcccatgg ttttaataaa tggtgctgag ggcattggta ctggatgggc ttgtaaacta 2640
cccaactatg atgctaggga aattgtgaac aatgtcagac gaatgctaga tggcctggat 2700
cctcatccca tgcttccaaa ctacaaaaac tttaaaggca cgattcaaga acttggtcaa 2760
aaccagtatg cagtcagtgg tgaaatattt gtagtggaca gaaacacagt agaaattaca 2820
gagcttccag ttagaacttg gacacaggta tataaagaac aggttttaga acctatgcta 2880
aatggaacag ataaaacacc agcattaatt tctgattata aagaatatca tactgacaca 2940
actgtgaaat ttgtggtgaa aatgactgaa gagaaactag cacaagcaga agctgctgga 3000
ctgcataaag tttttaaact tcaaactact cttacttgta attccatggt actttttgat 3060
catatgggat gtctgaagaa atatgaaact gtgcaagaca ttctgaaaga attctttgat 3120
ttacgattaa gttattacgg tttacgtaag gagtggcttg tgggaatgtt gggagcagaa 3180
tctacaaagc ttaacaatca agcccgtttc attttagaga agatacaagg gaaaattact 3240
atagagaata ggtcaaagaa agatttgatt caaatgttag tccagagagg ttatgaatct 3300
gacccagtga aagcctggaa agaagcacaa gaaaaggcag cagaagagga tgaaacacaa 3360
aaccagcatg atgatagttc ctccgattca ggaactcctt caggcccaga ttttaattat 3420
attttaaata tgtctctgtg gtctcttact aaagaaaaag ttgaagaact gattaaacag 3480
agagatgcaa aagggcgaga ggtcaatgat cttaaaagaa aatctccttc agatctttgg 3540
aaagaggatt tagcggcatt tgttgaagaa ctggataaag tggaatctca agaacgagaa 3600
gatgttctgg ctggaatgtc tggaaaagca attaaaggta aagttggcaa acctaaggtg 3660
aagaaactcc agttggaaga gacaatgccc tcaccttatg gcagaagaat aattcctgaa 3720
attacagcta tgaaggcaga tgccagcaaa aagttgctga agaagaagaa gggtgatctt 3780
gatactgcag cagtaaaagt ggaatttgat gaagaattca gtggagcacc agtagaaggt 3840
gcaggagaag aggcattgac tccatcagtt cctataaata aaggtcccaa acctaagagg 3900
gagaagaagg agcctggtac cagagtgaga aaaacaccta catcatctgg taaacctagt 3960
gcaaagaaag tgaagaaacg gaatccttgg tcagatgatg aatccaagtc agaaagtgat 4020
ttggaagaaa cagaacctgt ggttattcca agagattctt tgcttaggag agcagcagcc 4080
gaaagaccta aatacacatt tgatttctca gaagaagagg atgatgatgc tgatgatgat 4140
gatgatgaca ataatgattt agaggaattg aaagttaaag catctcccat aacaaatgat 4200
ggggaagatg aatttgttcc ttcagatggg ttagataaag atgaatatac attttcacca 4260
ggcaaatcaa aagccactcc agaaaaatct ttgcatgaca aaaaaagtca ggattttgga 4320
aatctcttct catttccttc atattctcag aagtcagaag atgattcagc taaatttgac 4380
agtaatgaag aagattctgc ttctgttttt tcaccatcat ttggtctgaa acagacagat 4440
aaagttccaa gtaaaacggt agctgctaaa aagggaaaac cgtcttcaga tacagtccct 4500
aagcccaaga gagccccaaa acagaagaaa gtagtagagg ctgtaaactc tgactcggat 4560

```
tcagaatttg gcattccaaa gaagactaca acaccaaaag gtaaaggccg aggggcaaag 4620
aaaaggaaag catctggctc tgaaaatgaa ggcgattata accctggcag gaaaacatcc 4680
aaaacaacaa gcaagaaacc gaagaagaca tcttttgatc aggattcaga tgtggacatc 4740
ttcccctcag acttccctac tgagccacct tctctgccac gaaccggtcg ggctaggaaa 4800
gaagtaaaat attttgcaga gtctgatgaa gaagaagatg atgttgattt tgcaatgttt 4860
aattaagtgc ccaaagagca caaacatttt tcaacaaata tcttgtgttg tccttttgtc 4920
ttctctgtct cagacttttg tacatctggc ttattttaat gtgatgatgt aattgacggt 4980
tttttattat tgtggtaggc cttttaacat tttgttctta cacatacagt tttatgctct 5040
tttttactca ttgaaatgtc acgtactgtc tgattggctt gtagaattgt tatagactgc 5100
cgtgcattag cacagatttt aattgtcatg gttacaaact acagacctgc tttttgaaat 5160
gaaatttaaa cattaaaaat ggaactgtg                                   5189
```

<210> 350
<211> 1536
<212> DNA
<213> Homo sapiens

<400> 350

```
gggggggggg ggaccacttg gcctgcctcc gtcccgccgc gccacttggc ctgcctccgt 60
cccgccgcgc cacttcgcct gcctccgtcc cccgcccgcc gcgccatgcc tgtggccggc 120
tcggagctgc cgcgccggcc cttgcccccc gccgcacagg agcgggacgc cgagccgcgt 180
ccgccgcacg gggagctgca gtacctgggg cagatccaac acatcctccg ctgcggcgtc 240
aggaaggacg accgcacggg caccggcacc ctgtcggtat tcggcatgca ggcgcgctac 300
agcctgagag atgaattccc tctgctgaca accaaacgtg tgttctggaa gggtgttttg 360
gaggagttgc tgtggtttat caagggatcc acaaatgcta aagagctgtc ttccaaggga 420
gtgaaaatct gggatgccaa tggatcccga gactttttgg acagcctggg attctccacc 480
agagaagaag gggacttggg cccagtttat ggcttccagt ggaggcattt tggggcagaa 540
tacagagata tggaatcaga ttattcagga cagggagttg accaactgca aagagtgatt 600
gacaccatca aaaccaaccc tgacgacaga agaatcatca tgtgcgcttg gaatccaaga 660
gatcttcctc tgatggcgct gcctccatgc catgccctct gccagttcta tgtggtgaac 720
agtgagctgt cctgccagct gtaccagaga tcgggagaca tgggcctcgg tgtgcctttc 780
aacatcgcca gctacgccct gctcacgtac atgattgcgc acatcacggg cctgaagcca 840
ggtgacttta tacacacttt gggagatgca catatttacc tgaatcacat cgagccactg 900
aaaattcagc ttcagcgaga acccagacct ttcccaaagc tcaggattct tcgaaaagtt 960
gagaaaattg atgacttcaa agctgaagac tttcagattg aagggtacaa tccgcatcca 1020
actattaaaa tggaaatggc tgtttagggt gctttcaaag gagcttgaag gatattgtca 1080
gtctttaggg gttgggctgg atgccgaggt aaaagttctt tttgctctaa aagaaaaagg 1140
aactaggtca aaaatctgtc cgtgacctat cagttattaa tttttaagga tgttgccact 1200
ggcaaatgta actgtgccag ttctttccat aataaaaggc tttgagttaa ctcactgagg 1260
gtatctgaca atgctgaggt tatgaacaaa gtgaggagaa tgaaatgtat gtgctcttag 1320
caaaaacatg tatgtgcatt tcaatcccac gtacttataa agaaggttgg tgaatttcac 1380
aagctatttt tggaatattt ttagaatatt ttaagaattt cacaagctat tccctcaaat 1440
ctgagggagc tgagtaacac catcgatcat gatgtagagt gtggttatga actttatagt 1500
tgttttatat gttgctataa taaagaagtg ttctgc                            1536
```

<210> 351
<211> 2386
<212> DNA
<213> Homo sapiens

<400> 351

```
ggaggaggaa gcaagcgagg gggctggttc ctgagcttcg caattcctgt gtcgccttct 60
gggctcccag cctgccgggt cgcatgatcc ctccggccgg agctggtttt tttgccagcc 120
accgcgaggc cggctgagtt accggcatcc ccgcagccac ctcctctccc gacctgtgat 180
acaaaagatc ttccgggggc tgcacctgcc tgcctttgcc taaggcggat ttgaatctct 240
ttctctccct tcagaatctt atcttggctt tggatcttag aagagaatca ctaaccagag 300
acgagactca gtgagtgagc aggtgttttg gacaatggac tggttgagcc catccctatt 360
ataaaaatgt ctcagagcaa ccgggagctg gtggttgact ttctctccta caagctttcc 420
cagaaaggat acagctggag tcagtttagt gatgtggaag agaacaggac tgaggcccca 480
gaagggactg aatcggagat ggagaccccc agtgccatca atggcaaccc atcctggcac 540
ctggcagaca gccccgcggt gaatggagcc actggccaca gcagcagttt ggatgcccgg 600
gaggtgatcc ccatggcagc agtaaagcaa gcgctgaggg aggcaggcga cgagtttgaa 660
ctgcggtacc ggcgggcatt cagtgacctg acatcccagc tccacatcac cccagggaca 720
gcatatcaga gctttgaaca ggatactttt gtggaactct atgggaacaa tgcagcagcc 780
gagagccgaa agggccagga acgcttcaac cgctggttcc tgacgggcat gactgtggcc 840
ggcgtggttc tgctgggctc actcttcagt cggaaatgac cagacactga ccatccactc 900
```

```
taccctccca ccccсttctc tgctccacca catcctccgt ccagccgcca ttgccaccag 960
gagaaccact acatgcagcc catgcccacc tgcccatcac agggttgggc ccagatctgg 1020
tcccttgcag ctagttttct agaatttatc acacttctgt gagaccccca cacctcagtt 1080
cccttggcct cagaattcac aaaatttcca caaaatctgt ccaaaggagg ctggcaggta 1140
tggaagggtt tgtggctggg ggcaggaggg ccctacctga ttggtgcaac ccttacccct 1200
tagcctccct gaaaatgttt ttctgccagg gagcttgaaa gttttcagaa cctcttcccc 1260
agaaaggaga ctagattgcc tttgttttga tgtttgtggc ctcagaattg atcattttcc 1320
ccccactctc cccacactaa cctgggttcc ctttccttcc atccctaccc cctaagagcc 1380
atttaggggc cacttttgac tagggattca ggctgcttgg gataaagatg caaggaccag 1440
gactccctcc tcacctctgg actggctaga gtcctcactc ccagtccaaa tgtcctccag 1500
aagcctctgg ctagaggcca gccccaccca ggagggaggg ggctatagct acaggaagca 1560
ccccatgcca aagctagggt ggcccttgca gttcagcacc accctagtcc cttcccctcc 1620
ctggctccca tgaccatact gagggaccaa ctgggcccaa gacagatgcc ccagagctgt 1680
ttatggcctc agctgcctca cttcctacaa gagcagcctg tggcatcttt gccttgggct 1740
gctcctcatg gtgggttcag gggactcagc cctgaggtga aagggagcta tcaggaacag 1800
ctatgggagc cccagggtct tccctacctc aggcaggaag ggcaggaagg agagcctgct 1860
gcatggggtg gggtagggct gactagaagg gccagtcctg cctggccagg cagatctgtg 1920
ccccatgcct gtccagcctg ggcagccagg ctgccaaggc cagagtggcc tggccaggag 1980
ctcttcaggc ctccctctct cttctgctcc acccttggcc tgtctcatcc ccaggggtcc 2040
cagccacccc gggctctctg ctgtacatat ttgagactag tttttattcc ttgtgaagat 2100
gatatactat ttttgttaag cgtgtctgta tttatgtgtg aggagctgct ggcttgcagt 2160
gcgcgtgcac gtggagagct ggtgcccgga gattggacgg cctgatgctc cctcccctgc 2220
cctggtccag ggaagctggc cgagggtcct ggctcctgag gggcatctgc ccctccccca 2280
acccccaccc cacacttgtt ccagctcttt gaaatagtct gtgtgaaggt gaaagtgcag 2340
ttcagtaata aactgtgttt actcagtgaa aaaaaaaaaa aaaaaa                2386

<210> 352
<211> 1270
<212> DNA
<213> Homo sapiens

<400> 352
agacgttcgc acacctgggt gccagcgccc cagaggtccc gggacagccc gaggcgccgc 60
gcccgccgcc ccgagctccc caagccttcg agagcggcgc acactcccgg tctccactcg 120
ctcttccaac acccgctcgt tttggcggca gctcgtgtcc cagagaccga gttgccccag 180
agaccgagac gccgccgctg cgaaggacca atgagagccc cgctgctacc gccggcgccg 240
gtggtgctgt cgctcttgat actcggctca ggccattatg ctgctggatt ggacctcaat 300
gacacctact ctgggaagcg tgaaccattt tctggggacc acagtgctga tggatttgag 360
gttacctcaa gaagtgagat gtcttcaggg agtgagattt cccctgtgag tgaaatgcct 420
tctagtagtg aaccgtcctc gggagccgac tatgactact cagaagagta tgataacgaa 480
ccacaaatac ctggctatat tgtcgatgat tcagtcagag ttgaacaggt agttaagccc 540
ccccaaaaca agacggaaag tgaaaatact tcagataaac ccaaaagaaa gaaaaaggga 600
ggcaaaaatg gaaaaaatag aagaaacaga aagaagaaaa atccatgtaa tgcagaattt 660
caaaatttct gcattcacgg agaatgcaaa tatatagagc acctggaagc agtaacatgc 720
aaatgtcagc aagaatattt cggtgaacgg tgtggggaaa agtccatgaa aactcacagc 780
atgattgaca gtagtttatc aaaaattgca ttagcagcca tagctgcctt tatgtctgct 840
gtgatcctca cagctgttgc tgttattaca gtccagctta gaagacaata cgtcaggaaa 900
tatgaaggag aagctgagga acgaaagaaa cttcgacaag agaatggaaa tgtacatgct 960
atagcataac tgaagataaa attacaggat atcacattgg agtcactgcc aagtcatagc 1020
cataaatgat gagtcggtcc tctttccagt ggatcataag acaatggacc ctttttgtta 1080
tgatggtttt aaactttcaa ttgtcacttt ttatgctatt tctgtatata aaggtgcacg 1140
aaggtaaaaa gtattttttc aagttgtaaa taatttattt aatatttaat ggaagtgtat 1200
ttatttaca gctcattaaa ctttttaac caaacagaaa aaaaaaaaaa aaaaaaaaaa 1260
aaaaaaaaaa                                                        1270

<210> 353
<211> 1600
<212> DNA
<213> Homo sapiens

<400> 353
gccccgccgc cggcagtgga ccgctgtgcg cgaaccctga accctacggt cccgacccgc 60
gggcgaggcc gggtacctgg gctgggatcc ggagcaagcg ggcgagggca gcgccctaag 120
caggcccgga gcgatggcag ccttgatgac cccgggaacc ggggccccac ccgcgcctgg 180
tgacttctcc ggggaaggga gccagggact tcccgaccct tcgccagagc ccaagcagct 240
cccggagctg atccgcatga agcgagacgg aggccgcctg agcgaagcgg acatcagggg 300
cttcgtggcc gctgtggtga atgggagcgc gcagggcgca cagatcgggg ccatgctgat 360
ggccatccga cttcggggca tggatctgga ggagacctcg gtgctgaccc aggccctggc 420
```

tcagtcggga cagcagctgg agtggccaga ggcctggcgc cagcagcttg tggacaagca 480
ttccacaggg ggtgtgggtg acaaggtcag cctggtcctc gcacctgccc tggcggcatg 540
tggctgcaag gtgccaatga tcagcggacg tggtctgggg cacacaggag gcaccttgga 600
taagctggag tctattcctg gattcaatgt catccagagc ccagagcaga tgcaagtgct 660
gctggaccag gcgggctgct gtatcgtggg tcagagtgag cagctggttc ctgcggacgg 720
aatcctatat gcagccagag atgtgacagc caccgtggac agcctgccac tcatcacagc 780
ctccattctc agtaagaaac tcgtggaggg gctgtccgct ctggtggtgg acgttaagtt 840
cggaggggcc gccgtcttcc ccaaccagga gcaggcccgg gagctggcaa agacgctggt 900
tggcgtggga gccagcctag ggcttcgggt cgcggcagcg ctgaccgcca tggacaagcc 960
cctgggtcgc tgcgtgggcc acgccctgga ggtggaggag gcgctgctct gcatggacgg 1020
cgcaggcccg ccagacttaa gggacctggt caccacgctc gggggcgccc tgctctggct 1080
cagcggacac gcggggactc aggctcaggg cgctgcccgg gtggccgcgg cgctggacga 1140
cggctcggcc cttggccgct tcgagcggat gctggcggcg cagggcgtgg atcccggtct 1200
ggcccgagcc ctgtgctcgg gaagtcccgc agaacgccgg cagctgctgc ctcgcgcccg 1260
ggagcaggag gagctgctgg cgcccgcaga tggcaccgtg gagctggtcc gggcgctgcc 1320
gctggcgctg gtgctgcacg agctcggggc cgggcgcagc cgcgctgggg agccgctccg 1380
cctgggggtg ggcgcagagc tgctggtcga cgtgggtcag aggctgcgcc gtgggacccc 1440
ctggctccgc gtgcaccggg acggccccgc gctcagcggc ccgcagagcc gcgccctgca 1500
ggaggcgctc gtactctccg accgcgcgcc attcgccgcc ccctcgccct tcgcagagct 1560
cgttctgccg ccgcagcaat aaagctcctt tgccgcgaaa 1600

<210> 354
<211> 1842
<212> DNA
<213> Homo sapiens

<400> 354
cgatcagatc gatctaagat ggcgactgtc gaaccggaaa ccacccctac tcctaatccc 60
ccgactacag aagaggagaa aacggaatct aatcaggagg ttgctaaccc agaacactat 120
attaaacatc ccctacagaa cagatgggca ctctggtttt ttaaaaatga taaaagcaaa 180
acttggcaag caaacctgcg gctgatctcc aagtttgata ctgttgaaga cttttgggct 240
ctgtacaacc atatccagtt gtctagtaat ttaatgcctg gctgtgacta ctcacttttt 300
aaggatggta ttgagcctat gtgggaagat gagaaaaaca aacggggagg acgatggcta 360
attacattga acaaacagca gagacgaagt gacctcgatc gcttttggct agagacactt 420
ctgtgcctta ttggagaatc ttttgatgac tacagtgatg atgtatgtgg cgctgttgtt 480
aatgttagag ctaaaggtga taagatagca atatggacta ctgaatgtga aaacagagaa 540
gctgttacac atatagggag ggtatacaag gaaaggttag gacttcctcc aaagatagtg 600
attggttatc agtcccacgc agacacagct actaagagcg gctccaccac taaaaatagg 660
tttgttgttt aagaagacac cttctgagta ttctcatagg agactgcgtc aagcaatcga 720
gatttgggag ctgaaccaaa gcctcttcaa aaagcagagt ggactgcatt taaatttgat 780
ttccatctta atgttactca gatataagag aagtctcatt cgcctttgtc ttgtacttct 840
gtgttcattt tttttttttt tttttggcta gagtttccac tatcccaatc aaagaattac 900
agtacacatc cccagaatcc ataaatgtgt tcctggccca ctctgtaata gttcagtaga 960
attaccatta attacataca gattttacct atccacaata gtcagaaaac aacttggcat 1020
ttctatactt tacaggaaaa aaaattctgt tgttccattt tatgcagaag catattttgc 1080
tggtttgaaa gattatgatg catacagttt tctagcaatt ttctttgttt ctttttacag 1140
cattgtcttt gctgtactct tgctgatggc tgctagattt taatttattt gtttccctac 1200
ttgataatat tagtgattct gatttcagtt tttcatttgt tttgcttaaa tttttttttt 1260
ttttttcctc atgtaacatt ggtgaaggat ccaggaatat gacacaaagg tggaataaac 1320
attaatttg tgcattcttt ggtaattttt tttgtttttt gtaactacaa agctttgcta 1380
caaatttatg catttcattc aaatcagtga tctatgtttg tgtgatttcc taaacataat 1440
tgtggattat aaaaaatgta acatcataat tacattccta actagaatta gtatgtctgt 1500
ttttgtatct ttatgctgta ttttaacact ttgtattact taggttattt tgctttggtt 1560
aaaaatggct caagtagaaa agcagtccca ttcatattaa gacagtgtac aaaactgtaa 1620
ataaaatgtg tacagtgaat tgtcttttag acaactagat ttgtcctttt atttctccat 1680
ctttatagaa ggaatttgta cttcttattg caggcaagtc tctatattat gtcctctttt 1740
gtggtgtctt ccatgtgaac agcataagtt tggagcacta gtttgattat tatgtttatt 1800
acaattttta ataaattgaa taggtagtat catatatatg ga 1842

<210> 355
<211> 4975
<212> DNA
<213> Homo sapiens

<400> 355
ctctcacaca cacacacccc tcccctgcca tccctccccg gactccggct ccggctccga 60
ttgcaatttg caacctccgc tgccgtcgcc gcagcagcca ccaattcgcc agcggttcag 120
gtggctcttg cctcgatgtc ctagcctagg ggcccccggg ccggacttgg ctgggctccc 180

ttcaccctct gcggagtcat gagggcgaac gacgctctgc aggtgctggg cttgcttttc 240
agcctggccc ggggctccga ggtgggcaac tctcaggcag tgtgtcctgg gactctgaat 300
ggcctgagtg tgaccggcga tgctgagaac caataccaga cactgtacaa gctctacgag 360
aggtgtgagg tggtgatggg gaaccttgag attgtgctca cgggacacaa tgccgacctc 420
tccttcctgc agtggattcg agaagtgaca ggctatgtcc tcgtggccat gaatgaattc 480
tctactctac cattgcccaa cctccgcgtg gtgcgaggga cccaggtcta cgatgggaag 540
tttgccatct tcgtcatgtt gaactataac accaactcca gccacgctct gcgccagctc 600
cgcttgactc agctcaccga gattctgtca ggggtgttt atattgagaa gaacgataag 660
ctttgtcaca tggacacaat tgactggagg gacatcgtga gggaccgaga tgctgagata 720
gtggtgaagg acaatggcag aagctgtccc ccctgtcatg aggtttgcaa ggggcgatgc 780
tggggtcctg gatcagaaga ctgccagaca ttgaccaaga ccatctgtgc tcctcagtgt 840
aatggtcact gctttgggcc caaccccaac cagtgctgcc atgatgagtg tgccgggggc 900
tgctcaggcc ctcaggacac agactgcttt gcctgccggc acttcaatga cagtggagcc 960
tgtgtacctc gctgtccaca gcctcttgtc tacaacaagc taactttcca gctggaaccc 1020
aatccccaca ccaagtatca gtatggagga gtttgtgtag ccagctgtcc ccataacttt 1080
gtggtggatc aaacatcctg tgtcagggcc tgtcctcctg acaagatgga agtagataaa 1140
aatgggctca agatgtgtga gccttgtggg ggactatgtc ccaaagcctg tgagggaaca 1200
ggctctggga gccgcttcca gactgtggac tcgagcaaca ttgatggatt tgtgaactgc 1260
accaagatcc tgggcaacct ggactttctg atcaccggcc tcaatggaga cccctggcac 1320
aagatccctg ccctggaccc agagaagctc aatgtcttcc ggacagtacg ggagatcaca 1380
ggttacctga acatccagtc ctggccgccc cacatgcaca acttcagtgt tttttccaat 1440
ttgacaacca ttggaggcag aagcctctac aaccggggct tctcattgtt gatcatgaag 1500
aacttgaatg tcacatctct gggcttccga tccctgaagg aaattagtgc tgggcgtatc 1560
tatataagtg ccaataggca gctctgctac caccactctt tgaactggac caaggtgctt 1620
cgggggccta cggaagagcg actagacatc aagcataatc ggccgcgcag agactgcgtg 1680
gcagagggca aagtgtgtga cccactgtgc tcctctgggg gatgctgggg cccaggccct 1740
ggtcagtgct tgtcctgtcg aaattatagc cgaggaggtg tctgtgtgac ccactgcaac 1800
tttctgaatg gggagcctcg agaatttgcc catgaggccg aatgcttctc ctgccacccg 1860
gaatgccaac ccatgggggg cactgccaca tgcaatggct cgggctctga tacttgtgct 1920
caatgtgccc attttcgaga tgggccccac tgtgtgagca gctgccccca tggagtccta 1980
ggtgccaagg gcccaatcta caagtaccca gatgttcaga atgaatgtcg gccctgccat 2040
gagaactgca cccaggggtg taaaggacca gagcttcaag actgtttagg acaaacactg 2100
gtgctgatcg gcaaaaccca tctgacaatg gctttgacag tgatagcagg attggtagtg 2160
attttcatga tgctgggcgg cacttttctc tactggcgtg ggcgccggat tcagaataaa 2220
agggctatga ggcgatactt ggaacggggt gagagcatag agcctctgga ccccagtgag 2280
aaggctaaca aagtcttggc cagaatcttc aaagagacag agctaaggaa gcttaaagtg 2340
cttggctcgg gtgtctttgg aactgtgcac aaaggagtgt ggatccctga gggtgaatca 2400
atcaagattc cagtctgcat taaagtcatt gaggacaaga gtggacggca gagttttcaa 2460
gctgtgacag atcatatgct ggccattggc agcctggacc atgcccacat tgtaaggctg 2520
ctgggactat gcccagggtc atctctgcag cttgtcactc aatatttgcc tctgggttct 2580
ctgctggatc atgtgagaca acaccggggg gcactggggc cacagctgct gctcaactgg 2640
ggagtacaaa ttgccaaggg aatgtactac cttgaggaac atggtatggt gcatagaaac 2700
ctggctgccc gaaacgtgct actcaagtca cccagtcagg ttcaggtggc agattttggt 2760
gtggctgacc tgctgcctcc tgatgataag cagctgctat acagtgaggc caagactcca 2820
attaagtgga tggcccttga gagtatccac tttgggaaat acacacacca gagtgatgtc 2880
tggagctatg gtgtgacagt ttgggagttg atgaccttcg gggcagagcc ctatgcaggg 2940
ctacgattgg ctgaagtacc agacctgcta gagaaggggg agcggttggc acagccccag 3000
atctgcacaa ttgatgtcta catggtgatg gtcaagtgtt ggatgattga tgagaacatt 3060
cgcccaacct ttaaagaact agccaatgag ttcaccagga tggcccgaga cccaccacgg 3120
tatctggtca taaagagaga gagtgggcct ggaatagccc ctgggccaga gccccatggt 3180
ctgacaaaca agaagctaga ggaagtagag ctggagccag aactagacct agacctagac 3240
ttggaagcag aggaggacaa cctggcaacc accacactgg gctccgccct cagcctacca 3300
gttggaacac ttaatcggcc acgtgggagc cagagccttt taagtccatc atctggatac 3360
atgcccatga accagggtaa tcttgggggg tcttgccagg agtctgcagt ttctgggagc 3420
agtgaacggt gcccccgtcc agtctctcta cacccaatgc cacggggatg cctggcatca 3480
gagtcatcag aggggcatgt aacaggctct gaggctgagc tccaggagaa agtgtcaatg 3540
tgtagaagcc ggagcaggag ccggagccca cggccacgcg gagatagcgc ctaccattcc 3600
cagcgccaca gtctgctgac tcctgttacc ccactctccc cacccgggtt agaggaagag 3660
gatgtcaacg gttatgtcat gccagataca cacctcaaag gtactccctc ctcccgggaa 3720
ggcacccttt cttcagtggg tctcagttct gtcctgggta ctgaagaaga agatgaagat 3780
gaggagtatg aatacatgaa ccggaggaga aggcacagtc cacctcatcc ccctaggcca 3840
agttcccttg aggagctggg ttatgagtac atggatgtgg ggtcagacct cagtgcctct 3900
ctgggcagca cacagagttg cccactccac cctgtaccca tcatgcccac tgcaggcaca 3960
actccagatg aagactatga atatatgaat cggcaacgag atggaggtgg tcctgggggt 4020
gattatgcag ccatgggggc ctgcccagca tctgagcaag ggtatgaaga gatgagagct 4080
tttcaggggc ctggacatca ggccccccat gtccattatg cccgcctaaa aactctacgt 4140
agcttagagg ctacagactc tgcctttgat aaccctgatt actggcatag caggcttttc 4200
cccaaggcta atgcccagag aacgtaactc ctgctccctg tggcactcag ggagcattta 4260

```
atggcagcta gtgcctttag agggtaccgt cttctcccta ttccctctct ctcccaggtc 4320
ccagcccctt ttccccagtc ccagacaatt ccattcaatc tttggaggct tttaaacatt 4380
ttgacacaaa attcttatgg tatgtagcca gctgtgcact ttcttctctt tcccaacccc 4440
aggaaaggtt ttccttattt tgtgtgcttt cccagtccca ttcctcagct tcttcacagg 4500
cactcctgga gatatgaagg attactctcc atatcccttc ctctcaggct cttgactact 4560
tggaactagg ctcttatgtg tgcctttgtt tcccatcaga ctgtcaagaa gaggaaaggg 4620
aggaaaccta gcagaggaaa gtgtaatttt ggtttatgac tcttaacccc ctagaaagac 4680
agaagcttaa aatctgtgaa gaaagaggtt aggagtagat attgattact atcataattc 4740
agcacttaac tatgagccag gcatcatact aaacttcacc tacattatct cacttagtcc 4800
tttatcatcc ttaaaacaat tctgtgacat acatattatc tcattttaca caaagggaag 4860
tcgggcatgg tggctcatgc ctgtaatctc agcactttgg gaggctgagg cagaaggatt 4920
acctgaggca aggagtttga gaccagctta gccaacatag taagaccccc atctc      4975
```

<210> 356
<211> 4627
<212> DNA
<213> Homo sapiens

<400> 356

```
tcacttgcct gatatttcca gtgtcagagg gacacagcca acgtggggtc ccttctaggc 60
tgacagccgc tctccagcca ctgccgcgag cccgtctgct cccgccctgc ccgtgcactc 120
tccgcagccg ccctccgcca agccccagcg cccgctccca tcgccgatga ccgcggggag 180
gaggatggag atgctctgtg ccggcagggt ccctgcgctg ctgctctgcc tgggtttcca 240
tcttctacag gcagtcctca gtacaactgt gattccatca tgtatcccag gagagtccag 300
tgataactgc acagctttag ttcagacaga agacaatcca cgtgtggctc aagtgtcaat 360
aacaaagtgt agctctgaca tgaatggcta ttgtttgcat ggacagtgca tctatctggt 420
ggacatgagt caaaactact gcaggtgtga agtgggttat actggtgtcc gatgtgaaca 480
cttcttttta accgtccacc aaccttttaag caaagagtat gtggctttga ccgtgattct 540
tattattttg tttcttatca cagtcgtcgg ttccacatat tatttctgca gatggtacag 600
aaatcgaaaa agtaaagaac caaagaagga atatgagaga gttacctcag gggatccaga 660
gttgccgcaa gtctgaatgg cgccatcaaa cttatgggca gggataacag tgtgcctggt 720
taatattaat attccatttt attaataata tttatgttgg gtcaagtgtt aggtcaataa 780
cactgtattt taatgtactt gaaaaatgtt tttatttttg ttttattttt gacagactat 840
ttgctaatgt ataatgtgca gaaaatattt aatatcaaaa gaaaattgat atttttatac 900
aagtaatttc ctgagctaaa tgcttcattg aaagcttcaa agtttatatg cctggtgcac 960
agtgcttaga agtaagcaat tcccaggtca tagctcaaga attgttagca aatgacagat 1020
ttctgtaagc ctatatatat agtcaaatcg atttagtaag tatgtttttt atgttcctca 1080
aatcagtgat aattggtttg actgtaccat ggtttgatat gtagttggca ccatggtatc 1140
atatattaaa acaataatgc aattagaatt tgggagaagc aaatataggt cctgtgttaa 1200
acactacaca tttgaaacaa gctaaccctg ggagtctat ggtctcttca ctcaggtctc 1260
agctataatt ctgttatatg aggggcagtg gacagttccc tatgccaact cacgactcct 1320
acaggtacta gtcactcatc taccagattc tgcctatgta aaatgaattg aaaaacaatt 1380
ttctgtaatc ttttatttaa gtagtgggca tttcatagct tcacaatgtt cctttttgt 1440
atattacaac atttatgtga ggtaattatt gctcaacaga caattagaaa aaagtccaca 1500
cttgaagcct aaatttgtgc tttttaagaa tatttttaga ctatttcttt ttataggggc 1560
tttgctgaat tctaacatta aatcacagcc caaaatttga tggactaatt attattttaa 1620
aatatatgaa gacaataatt ctacatgttg tcttaagatg gaaatacagt tatttcatct 1680
tttattcaag gaagttttaa ctttaataca gctcagtaaa tggcttcttc tagaatgtaa 1740
agttatgtat ttaaagttgt atcttgacac aggaaatggg aaaaaactta aaaattaata 1800
tggtgtattt ttccaaatga aaaatctcaa ttgaaagctt ttaaaatgta gaaacttaaa 1860
cacaccttcc tgtggaggct gagatgaaaa ctagggctca ttttcctgac atttgtttat 1920
tttttggaag agacaaagat ttcttctgca ctctgagccc ataggtctca gagagttaat 1980
aggagtattt ttgggctatt gcataaggag ccactgctgc caccactttt ggattttatg 2040
ggaggctcct tcatcgaatg ctaaaccttt gagtagagtc tccctggatc acataccagg 2100
tcagggagga tctgttcttc ctctacgttt atcctggcat gtgctagggt aaacgaaggc 2160
ataataagcc atggctgacc tctggagcac caggtgccag gacttgtctc catgtgtatc 2220
catgcattat ataccctggt gcaatcacac gactgtcatc taaagtcctg gccctggccc 2280
ttactattag gaaaataaac agacaaaaac aagtaaatat atatggtcct atacatattg 2340
tatatatatt catatacaaa catgtatgta tacatgacct taatggatca tagaattgca 2400
gtcatttggt gctctgctaa ccatttatat aaaacttaaa aacaagagaa aagaaaaatc 2460
aattagatct aaacagttat ttctgtttcc tatttaatat agctgaagtc aaaatatgta 2520
agaacacatt ttaaatactc tacttacagt tggccctctg tggttagttc cacatctgtg 2580
gattcaacca accaaggacg gaaaatgctt aaaaaataat acaacaacaa caaaaaatac 2640
attataacaa ctatttactt tttttttttt ctttttgaga tggagtctcg ctctgttgcc 2700
caggttggag tgcagtggca cgatctcggc tcactgcaac ctcacctccc gggttcaaga 2760
gatcctcctg cctcagcctc ctgagcagct gggactacag gcgcatgcca ccatgcccag 2820
ctaatttttg tatttttagt agaggcgggg tttcaccatg ttggccagga tggtctcaat 2880
ctcctaacct tgagatccac cctccacagc ctcccaaact gctgggatta caggcgtgag 2940
```

ccaccgcacg tagcatttac attaggtatt acaagtaatg taaagatgat ttaagtatac 3000
aggaggatgt gaataggtta tatgcaagca ctatgccctt ttatataagt gacttgaaca 3060
tctgtgcccg attttagtat gtgcaggggg gcgatctggg aatcagtccc ctgtggatac 3120
caaggtacaa ctgtatttat taacgcttac tagatgtgag gagagtctga atattttcag 3180
tgatcttggc tgtttcaaaa aaatctattg acttttcaat aaatcagctg caatccattt 3240
atttcattta caaaagattt attgtaagcc tctcaatctt ggtttttcag ttgatcttaa 3300
gcatgtcaat tcataaaaac aagtcatttt tgtatttttc atctttaaga atgcttaaaa 3360
aagctaatcc ctaaaatagt tagatctttg taaatgcata ttaaataata aagtatgacc 3420
cacattactt tttatgggtg aaaataagac aaaaataata gttttagtga ggatggtgct 3480
gagtaaacat aaaaactgat ttgctctcag ctgatgtgtc ctgtacacag tgggaagatt 3540
ttagttcaca cttagtctaa ctcccccatt ttacagattt ctcactatat atatttctag 3600
aaggggctat gcatattcaa tgtattgaga accaaagcaa ccacaaatgc ataaatgcat 3660
aatttatggt cttcaaccaa ggccacataa taacccagtt aacttactct ttaaccagga 3720
atattaagtt ctataactag tactcaaggt ttaaccttaa aattaagatt tccttaacct 3780
taaccttaaa attgatatta tattaaacat acataataca atgtaactcc actgttctcc 3840
tgaatatttt ttgctctaat ctctctgccg aaagtcaaag tgatgggaga attggtatac 3900
tggtatgact acgtcttaag tcagattttt atttatgagt ctttgagact aaattcaatc 3960
accaccaggt atcaaatcaa cttttatgca gcaaatatat gattctagtg tctgactttt 4020
gttaaattca gtaatgcagt ttttaaaaac ctgtatctga cccactttgt aatttttgct 4080
ccaatatcca ttctgtagac ttttgaaaaa aaagttttta atttgatgcc caatatattc 4140
tgaccgttaa aaaattcttg ttcatatggg agaaggggga gtaatgactt gtacaaacag 4200
tatttctggt gtatatttta atgtttttaa aaagagtaat ttcatttaaa tatctgttat 4260
tcaaatttga tgatgttaaa tgtaatataa tgtatttttct ttttattttg cactctgtaa 4320
ttgcactttt taagtttgaa gagccatttt ggtaaacggt ttttattaaa gatgctatgg 4380
aacataaagt tgtattgcat gcaatttaaa gtaacttatt tgactatgaa tattatcgga 4440
ttactgaatt gtatcaattt gtttgtgttc aatatcagct ttgataattg tgtaccttaa 4500
gatattgaag gagaaaatag ataatttaca agatattatt aatttttatt tatttttctt 4560
gggaattgaa aaaaattgaa ataaataaaa atgcattgaa catcttgcat tcaaaatctt 4620
cactgac 4627

<210> 357
<211> 2634
<212> DNA
<213> Homo sapiens

<400> 357
ggcacgaggc tgagtgtccg tctcgcgccc ggaagcgggc gaccgccgtc agcccggagg 60
aggaggagga ggaggaggag gagggggcgg ccatggggct gctgtcccag ggctcgccgc 120
tgagctggga ggaaaccaag cgccatgccg accacgtgcg gcggcacggg atcctccagt 180
tcctgcacat ctaccacgcc gtcaaggacc ggcacaagga cgttctcaag tggggcgatg 240
aggtggaata catgttggta tcttttgatc atgaaaataa aaaagtccgg ttggtcctgt 300
ctggggagaa agttcttgaa actctgcaag agaaggggga aaggacaaac ccaaaccatc 360
ctaccctttg gagaccagag tatgggagtt acatgattga agggacacca ggacagccct 420
acggaggaac aatgtccgag ttcaatacag ttgaggccaa catgcgaaaa cgccggaagg 480
aggctacttc tatattagaa gaaaatcagg ctctttgcac aataacttca tttcccagat 540
taggctgtcc tgggttcaca ctgcccgagg tcaaacccaa cccagtggaa ggaggagctt 600
ccaagtccct cttctttcca gatgaagcaa taaacaagca ccctcgcttc agtaccttaa 660
caagaaatat ccgacatagg agaggagaaa aggttgtcat caatgtacca atatttaagg 720
acaagaatac accatctcca tttatagaaa catttactga ggatgatgaa gcttcaaggg 780
cttctaagcc ggatcatatt tacatggatg ccatgggatt tggaatgggc aattgctgtc 840
tccaggtgac attccaagcc tgcagtatat ctgaggccag ataccttat gatcagttgg 900
ctactatctg tccaattgtt atggctttga gtgctgcatc tccctttac cgaggctatg 960
tgtcagacat tgattgtcgc tggggagtga tttctgcatc tgtagatgat agaactcggg 1020
aggagcgagg actggagcca ttgaagaaca ataactatag gatcagtaaa tcccgatatg 1080
actcaataga cagctattta tctaagtgtg gtgagaaata taatgacatc gacttgacga 1140
tagataaaga gatctacgaa cagctgttgc aggaaggcat tgatcatctc ctggcccagc 1200
atgttgctca tctctttatt agagacccac tgacactgtt tgaagagaaa atacacctgg 1260
atgatgctaa tgagtctgac cattttgaga atattcagtc cacaaattgg cagacaatga 1320
gatttaagcc ccctcctcca aactcagaca ttggatggag agtagaattt cgacccatgg 1380
aggtgcaatt aacagacttt gagaactctg cctatgtggt gtttgtggta ctgctcacca 1440
gagtgatcct ttcctacaaa ttggattttc tcattccact gtcaaaggtt gatgagaaca 1500
tgaaggtagc acagaaaaga gatgctgtct tgcagggaat gttttatttc aggaaagata 1560
tttgcaaagg tggcaatgca gtggtggatg gttgtggcaa ggcccagaac agcacggagc 1620
tcgctgcaga ggagtacacc ctcatgagca tagacaccat catcaatggg aaggaaggtg 1680
tgtttcctgg actgatccca attctgaact cttaccttga aaacatggaa gtggatgtgg 1740
acaccagatg tagtattctg aactacctaa agctaattaa gaagagagca tctggagaac 1800
taatgacagt tgccagatgg atgagggagt ttatcgcaaa ccatcctgac tacaagcaag 1860
acagtgtcat aactgatgaa atgaattata gccttatttt gaagtgtaac caaattgcaa 1920

atgaattatg tgaatgccca gagttacttg gatcagcatt taggaaagta aaatatagtg 1980
gaagtaaaac tgactcatcc aactagacat tctacagaaa gaaaaatgca ttattgacga 2040
actggctaca gtaccatgcc tctcagcccg tgtgtataat atgaagacca aatgatagaa 2100
ctgtactgtt ttctgggcca gtgagccaga aattgattaa ggctttcttt ggtaggtaaa 2160
tctagagttt atacagtgta catgtacata gtaaagtatt tttgattaac aatgtatttt 2220
aataacatat ctaaagtcat catgaactgg cttgtacatt tttaaattct tactctggag 2280
caacctactg tctaagcagt tttgtaaatg tactggtaat tgtacaatac ttgcattcca 2340
gagttaaaat gtttactgta aatttttgtt cttttaaaga ctacctggga cctgatttat 2400
tgaaattttt ctctttaaaa acattttctc tcgttaattt tcctttgtca tttcctttgt 2460
tgtctacatt aaatcacttg aatccattga aagtgcttca agggtaatct tgggtttcta 2520
gcaccttatc tatgatgttt cttttgcaat tggaataatc acttggtcac cttgccccaa 2580
gctttcccct ctgaataaat acccattgaa ctctgaaaaa aaaaaaaaaa aaaa 2634

<210> 358
<211> 1246
<212> DNA
<213> Homo sapiens

<400> 358
gaccagccta cagccgcctg catctgtatc cagcgccagg tcccgccagt cccagctgcg 60
cgcgcccccc agtcccgcac ccgttcggcc caggctaagt tagccctcac catgccggtc 120
aaaggaggca ccaagtgcat caaatacctg ctgttcggat ttaacttcat cttctggctt 180
gccgggattg ctgtccttgc cattggacta tggctccgat tcgactctca gaccaagagc 240
atcttcgagc aagaaactaa taataataat tccagcttct acacaggagt ctatattctg 300
atcggagccg gcgccctcat gatgctggtg ggcttcctgg gctgctgcgg ggctgtgcag 360
gagtcccagt gcatgctggg actgttcttc ggcttcctct tggtgatatt cgccattgaa 420
atagctgcgg ccatctgggg atattcccac aaggatgagg tgattaagga agtccaggag 480
ttttacaagg acacctacaa caagctgaaa accaaggatg agccccagcg ggaaacgctg 540
aaagccatcc actatgcgtt gaactgctgt ggtttggctg gggcgtggaa acagtttatc 600
tcagacatct gccccaagaa ggacgtactc gaaaccttca ccgtgaagtc ctgtcctgat 660
gccatcaaag aggtcttcga caataaattc cacatcatcg gcgcagtggg catcggcatt 720
gccgtggtca tgatatttgg catgatcttc agtatgatct tgtgctgtgc tatccgcagg 780
aaccgcgaga tggtctagag tcagcttaca tccctgagca ggaaagttta cccatgaaga 840
ttggtgggat tttttgtttg tttgttttgt tttgtttgtt gtttgttgtt tgtttttttg 900
ccactaattt tagtattcat tctgcattgc tagataaaag ctgaagttac tttatgtttg 960
tcttttaatg cttcattcaa tattgacatt tgtagttgag cggggggttt ggtttgcttt 1020
ggtttatatt ttttcagttg tttgtttttg cttgttatat taagcagaaa tcctgcaatg 1080
aaaggtacta tatttgctag actctagaca agatattgta cataaaagaa ttttttttgtc 1140
tttaaataga tacaaatgtc tatcaacttt aatcaagttg taacttatat tgaagacaat 1200
ttgatacata ataaaaaatt atgacaatgt caaaaaaaaa aaaaaa 1246

<210> 359
<211> 2360
<212> DNA
<213> Homo sapiens

<400> 359
gctacgcggg ccacgctgct ggctggcctg acctaggcgc gcggggtcgg gcggccgcgc 60
gggcgggctg agtgagcaag acaagacact caagaagagc gagctgcgcc tgggtcccgg 120
ccaggcttgc acgcagaggc gggcggcaga cggtgcccgg cggaatctcc tgagctccgc 180
cgcccagctc tggtgccagc gcccagtggc cgccgcttcg aaagtgactg gtgcctcgcc 240
gcctcctctc ggtgcgggac catgaagctg ctgccgtcgg tggtgctgaa gctctttctg 300
gctgcagttc tctcggcact ggtgactggc gagagcctgg agcggcttcg gagagggcta 360
gctgctggaa ccagcaaccc ggaccctccc actgtatcca cggaccagct gctacccccta 420
ggaggcggcc gggaccggaa agtccgtgac ttgcaagagg cagatctgga ccttttgaga 480
gtcactttat cctccaagcc acaagcactg gccacaccaa acaaggagga gcacgggaaa 540
agaaagaaga aaggcaaggg gctagggaag aagagggacc catgtcttcg gaaatacaag 600
gacttctgca tccatggaga atgcaaatat gtgaaggagc tccgggctcc ctcctgcatc 660
tgccacccgg gttaccatgg agagaggtgt catgggctga gcctcccagt ggaaaatcgc 720
ttatataccт atgaccacac aaccatcctg gccgtggtgg ctgtggtgct gtcatctgtc 780
tgtctgctgg tcatcgtggg gcttctcatg tttaggtacc ataggagagg aggttatgat 840
gtggaaaatg aagagaaagt gaagttgggc atgactaatt cccactgaga gagacttgtg 900
ctcaaggaat cggctgggga ctgctacctc tgagaagaca caaggtgatt tcagactgca 960
gaggggaaag acttccatct agtcacaaag actccttcgt ccccagttgc cgtctaggat 1020
tgggcctccc ataattgctt tgccaaaata ccagagcctt caagtgccaa acagagtatg 1080
tccgatggta tctgggtaag aagaaagcaa aagcaaggga ccttcatgcc cttctgattc 1140
ccctccacca aaccccactt cccctcataa gtttgtttaa acacttatct tctggattag 1200
aatgccggtt aaattccata tgctccagga tctttgactg aaaaaaaaaa agaagaagaa 1260

gaaggagagc aagaaggaaa gatttgtgaa ctggaagaaa gcaacaaaga ttgagaagcc 1320
atgtactcaa gtaccaccaa gggatctgcc attgggaccc tccagtgctg gatttgatga 1380
gttaactgtg aaataccaca agcctgagaa ctgaattttg ggacttctac ccagatggaa 1440
aaataacaac tatttttgtt gttgttgttt gtaaatgcct cttaaattat atatttattt 1500
tattctatgt atgttaattt atttagtttt taacaatcta acaataatat ttcaagtgcc 1560
tagactgtta ctttggcaat ttcctggccc tccactcctc atccccacaa tctggcttag 1620
tgccacccac ctttgccaca aagctaggat ggttctgtga cccatctgta gtaatttatt 1680
gtctgtctac atttctgcag atcttccgtg gtcagagtgc cactgcggga gctctgtatg 1740
gtcaggatgt aggggttaac ttggtcagag ccactctatg agttggactt cagtcttgcc 1800
taggcgattt tgtctaccat ttgtgttttg aaagcccaag gtgctgatgt caaagtgtaa 1860
cagatatcag tgtctccccg tgtcctctcc ctgccaagtc tcagaagagg ttgggcttcc 1920
atgcctgtag ctttcctggt ccctcacccc catggcccca ggccacagcg tgggaactca 1980
ctttcccttg tgtcaagaca tttctctaac tcctgccatt cttctggtgc tactccatgc 2040
aggggtcagt gcagcagagg acagtctgga gaaggtatta gcaaagcaaa aggctgagaa 2100
ggaacaggga acattggagc tgactgttct tggtaactga ttacctgcca attgctaccg 2160
agaaggttgg aggtggggaa ggctttgtat aatcccaccc acctcaccaa aacgatgaag 2220
gtatgctgtc atggtccttt ctggaagttt ctggtgccat ttctgaactg ttacaacttg 2280
tatttccaaa cctggttcat atttatactt tgcaatccaa ataaagataa cccttattcc 2340
ataaaaaaaa aaaaaaaaaa 2360

<210> 360
<211> 1433
<212> DNA
<213> Homo sapiens

<400> 360
attcggggcg agggaggagg aagaagcgga ggaggcggct cccgctcgca gggccgtgca 60
cctgcccgcc cgcccgctcg ctcgctcgcc cgccgcgccg cgctgccgac cgccagcatg 120
ctgccgagag tgggctgccc cgcgctgccg ctgccgccgc cgccgctgct gccgctgctg 180
ccgctgctgc tgctgctact gggcgcgagt ggcggcggcg gcggggcgcg cgcggaggtg 240
ctgttccgct gcccgccctg cacacccgag cgcctggccg cctgcgggcc cccgccggtt 300
gcgccgcccg ccgcggtggc cgcagtggcc ggaggcgccc gcatgccatg cgcggagctc 360
gtccgggagc cgggctgcgg ctgctgctcg gtgtgcgccc ggctggaggg cgaggcgtgc 420
ggcgtctaca ccccgcgctg cggccagggg ctgcgctgct atccccaccc gggctccgag 480
ctgcccctgc aggcgctggt catgggcgag ggcacttgtg agaagcgccg ggacgccgag 540
tatggcgcca gcccggagca ggttgcagac aatggcgatg accactcaga aggaggcctg 600
gtggagaacc acgtggacag caccatgaac atgttgggcg ggggaggcag tgctggccgg 660
aagcccctca agtcgggtat gaaggagctg gccgtgttcc gggagaaggt cactgagcag 720
caccggcaga tgggcaaggg tggcaagcat caccttggcc tggaggagcc caagaagctg 780
cgaccacccc ctgccaggac tccctgccaa caggaactgg accaggtcct ggagcggatc 840
tccaccatgc gccttccgga tgagcggggc cctctggagc acctctactc cctgcacatc 900
cccaactgtg acaagcatgg cctgtacaac ctcaaacagt gcaagatgtc tctgaacggg 960
cagcgtgggg agtgctggtg tgtgaacccc aacaccggga agctgatcca gggagccccc 1020
accatccggg gggaccccga gtgtcatctc ttctacaatg agcagcagga ggcttgcggg 1080
gtgcacaccc agcggatgca gtagaccgca gccagccggt gcctggcgcc cctgcccccc 1140
gcccctctcc aaacaccggc agaaaacgga gagtgcttgg gtggtgggtg ctggaggatt 1200
ttccagttct gacacacgta tttatatttg gaaagagacc agcaccgagc tcggcacctc 1260
cccggcctct ctcttcccag ctgcagatgc cacacctgct ccttcttgct ttccccgggg 1320
gaggaagggg gttgtggtcg ggagctgggg gtacaggttt ggggaggggg aagagaaatt 1380
tttatttttg aaccccctgtg tccctttttgc ataagattaa aggaaggaaa agt 1433

<210> 361
<211> 1632
<212> DNA
<213> Homo sapiens

<400> 361
gccggccgaa cccagacccg aggttttaga agcagagtca ggcgaagctg ggccagaacc 60
gcgacctccg caaccttgag cggcatccgt ggagtgcgcc tgcgcagcta cgaccgcagc 120
aggaaagcgc cgccggccag gcccagctgt ggccggacag ggactggaag agaggacgcg 180
gtcgagtagg tgtgcaccag ccctggcaac gagagcgtct accccgaact ctgctggcct 240
tgaggtgggg aagccgggga gggcagttga ggaccccgcg gaggcgcgtg actggttgag 300
cgggcaggcc agcctccgag ccgggtggac acaggtttta aaacatgaat cctacactca 360
tccttgctgc cttttgcctg ggaattgcct cagctactct aacatttgat cacagtttag 420
aggcacagtg gaccaagtgg aaggcgatgc acaacagatt atacggcatg aatgaagaag 480
gatggaggag agcagtgtgg gagaagaaca tgaagatgat tgaactgcac aatcaggaat 540
acagggaagg gaaacacagc ttcacaatgg ccatgaacgc ctttggagac atgaccagtg 600
aagaattcag gcaggtgatg aatggctttc aaaaccgtaa gcccaggaag ggaaagtgt 660

```
tccaggaacc tctgttttat gaggccccca gatctgtgga ttggagagag aaaggctacg 720
tgactcctgt gaagaatcag ggtcagtgtg gttcttgttg ggcttttagt gctactggtg 780
ctcttgaagg acagatgttc cggaaaactg ggaggcttat ctcactgagt gagcagaatc 840
tggtagactg ctctgggcct caaggcaatg aaggctgcaa tggtggccta atggattatg 900
ctttccagta tgttcaggat aatggaggcc tggactctga ggaatcctat ccatatgagg 960
caacagaaga atcctgtaag tacaatccca agtattctgt tgctaatgac accggctttg 1020
tggacatccc taagcaggag aaggccctga tgaaggcagt tgcaactgtg gggcccattt 1080
ctgttgctat tgatgcaggt catgagtcct tcctgttcta taaagaaggc atttattttg 1140
agccagactg tagcagtgaa gacatggatc atggtgtgct ggtggttggc tacggatttg 1200
aaagcacaga atcagataac aataaatatt ggctggtgaa gaacagctgg ggtgaagaat 1260
ggggcatggg tggctacgta aagatggcca aagaccggag aaaccattgt ggaattgcct 1320
cagcagccag ctaccccact gtgtgagctg gtggacggtg atgaggaagg acttgactgg 1380
ggatggcgca tgcatgggag gaattcatct tcagtctacc agcccccgct gtgtcggata 1440
cacactcgaa tcattgaaga tccgagtgtg atttgaattc tgtgatattt tcacactggt 1500
aaatgttacc tctattttaa ttactgctat aaataggttt atattattga ttcacttact 1560
gactttgcat tttcgttttt aaaaggatgt ataaattttt acctgtttaa ataaaattta 1620
atttcaaatg ta                                                     1632
```

<210> 362
<211> 2756
<212> DNA
<213> Homo sapiens

<400> 362

```
atgctgtcct tccagtaccc cgacgtgtac cgcgacgaga ccgccgtaca ggattatcat 60
ggtcataaaa tttgtgaccc ttacgcctgg cttgaagacc ccgacagtga acagactaag 120
gcctttgtgg aggcccagaa taagattact gtgccatttc ttgagcagtg tcccatcaga 180
ggtttataca aagagagaat gactgaacta tatgattatc ccaagtatag ttgccacttc 240
aagaaaggaa aacggtattt ttatttttac aatacaggtt tgcagaacca gcgagtatta 300
tatgtacagg attccttaga gggtgaggcc agagtgttcc tggaccccaa catactgtct 360
gacgatggca cagtggcact ccgaggttat gcgttcagcg aagatggtga atattttgcc 420
tatggtctga gtgccagtgg ctcagactgg gtgacaatca agttcatgaa agttgatggt 480
gccaaagagc ttccagatgt gcttgaaaga gtcaagttca gctgtatggc ctggacccat 540
gatgggaagg gaatgttcta caactcatac cctcaacagg atggaaaaag tgatggcaca 600
gagacatcta ccaatctcca ccaaaagctc tactaccatg tcttgggaac cgatcagtca 660
gaagatattt tgtgtgctga gtttcctgat gaacctaaat ggatgggtgg agctgagtta 720
tctgatgatg gccgctatgt cttgttatca ataagggaag gatgtgatcc agtaaaccga 780
ctctggtact gtgacctaca gcaggaatcc agtggcatcg cgggaatcct gaagtgggta 840
aaactgattg acaactttga aggggaatat gactacgtga ccaatgaggg ggcggtgttc 900
acattcaaga cgaatcgcca gtctcccaac tatcgcgtga tcaacattga cttcagggat 960
cctgaagagt ctaagtggaa agtacttgtt cctgagcatg agaaagatgt cttagaatgg 1020
atagcttgtg tcaggtccaa cttcttggtc ttatgctacc tccatgacgt caagaacatt 1080
ctgcagctcc atgacctgac tactggtgct ctccttaaga ccttcccgct cgatgtcggc 1140
agcattgtag ggtacagcgg tcagaagaag gacactgaaa tcttctatca gtttacttcc 1200
tttttatctc caggtatcat ttatcactgt gatcttacca aagaggagct ggagccaaga 1260
gttttccgag aggtgaccgt aaaaggaatt gatgcttctg attaccagac agtccagatt 1320
ttctacccta gcaaggatgg tacgaagatt ccaatgttca ttgtgcataa aaaaagcata 1380
aaattggatg gctctcatcc agctttctta tatggctatg gcggcttcaa catatccatc 1440
acacccaact acagtgtttc caggcttatt tttgtgagac acatgggtgg tatcctggca 1500
gtggccaaca tcagaggagg tggcgaatat ggagagacgt ggcataaagg tggtatcttg 1560
gccaacaaac aaaactgctt tgatgacttt cagtgtgctg ctgagtatct gatcaaggaa 1620
ggttacacat ctcccaagag gctgactatt aatggaggtt caaatggagg cctcttagtg 1680
gctgcttgtg caaatcagag acctgacctc tttggttgtg ttattgccca agttggagta 1740
atggacatgc tgaagtttca taaatatacc atcggccatg cttggaccac tgattatggg 1800
tgctcggaca gcaaacaaca ctttgaatgg cttgtcaaat actctccatt gcataatgtg 1860
aagttaccag aagcagatga catccagtac ccgtccatgc tgctcctcac tgctgaccat 1920
gatgaccgcg tggtcccgct tcactccctg aagttcattg ccacccttca gtacatcgtg 1980
ggccgcagca ggaagcaaag caaccccctg cttatccacg tggacaccaa ggcgggccac 2040
ggggcgggga agcccacagc caaagtgata gaggaagtct cagacatgtt tgcgttcatc 2100
gcgcggtgcc tgaacgtcga ctggattcca taaacagttt tcgtgcttcc tcctgacagc 2160
gacagaaaac ctcaagggct ttcccacgtt gacaccaaga aaccactggg cataatgctt 2220
ccccacggga acattattcc tggactgaca ggctacagtt gaacagaact gccgtgggaa 2280
ttttatcttt tttaggcttc tcctttttag caaggccttg gtgtttcttt ttccaccctg 2340
tctaggcaca tgtggttttt tggtgttttt tttaagggca tgttgggata aatagctaaa 2400
tggcaacaaa cacattgtga atattagatt gctgaattaa ggatcatagt cgggcatact 2460
tatctatatc cataacctct atatctttaa ataaatgtga gaactgttct catggagaag 2520
acttctttgc aacaataata aatgttattt aagaatgaca gggatttact tccggtttct 2580
tcatattgag gggcaactcc agaagtggag ttttctgtga gaataaagca tttcaccttt 2640
```

ctgcaacaag ttagttttca agcagttaag tcatagaatg tttgttagct gtgaaaataa 2700
gttgttcatc caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaag gaattc 2756

<210> 363
<211> 2768
<212> DNA
<213> Homo sapiens

<400> 363
cactgctgtg cagggcagga aagctccatg cacatagccc agcaaagagc aacacagagc 60
tgaaaggaag actcagagga gagagataag taaggaaagt agtgatggct ctcatcccag 120
acttggccat ggaaacctgg cttctcctgg ctgtcagcct ggtgctcctc tatctatatg 180
gaacccattc acatggactt tttaagaagc ttggaattcc agggcccaca cctctgcctt 240
ttttgggaaa tattttgtcc taccataagg gcttttgtat gtttgacatg gaatgtcata 300
aaaagtatgg aaaagtgtgg ggcttttatg atggtcaaca gcctgtgctg gctatcacag 360
atcctgacat gatcaaaaca gtgctagtga aagaatgtta ttctgtcttc acaaaccgga 420
ggcctttgg tccagtggga tttatgaaaa gtgccatctc tatagctgag gatgaagaat 480
ggaagagatt acgatcattg ctgtctccaa ccttcaccag tggaaaactc aaggagatgg 540
tccctatcat tgcccagtat ggagatgtgt tggtgagaaa tctgaggcgg gaagcagaga 600
caggcaagcc tgtcaccttg aaagacgtct ttggggccta cagcatggat gtgatcacta 660
gcacatcatt tggagtgaac atcgactctc tcaacaatcc acaagacccc tttgtggaaa 720
acaccaagaa gcttttaaga tttgattttt tggatccatt ctttctctca ataacagtct 780
ttccattcct catcccaatt cttgaagtat taaatatctg tgtgtttcca agagaagtta 840
caaatttttt aagaaaatct gtaaaaagga tgaaagaaag tcgcctcgaa gatacacaaa 900
agcaccgagt ggatttcctt cagctgatga ttgactctca gaattcaaaa gaaactgagt 960
cccacaaagc tctgtccgat ctggagctcg tggcccaatc aattatcttt atttttgctg 1020
gctatgaaac cacgagcagt gttctctcct tcattatgta tgaactggcc actcaccctg 1080
atgtccagca gaaactgcag gaggaaattg atgcagtttt acccaataag gcaccaccca 1140
cctatgatac tgtgctacag atggagtatc ttgacatggt ggtgaatgaa acgctcagat 1200
tattcccaat tgctatgaga cttgagaggg tctgcaaaaa agatgttgag atcaatggga 1260
tgttcattcc caaaggggtg gtggtgatga ttccaagcta tgctcttcac cgtgacccaa 1320
agtactggac agagcctgag aagttcctcc ctgaaagatt cagcaagaag aacaaggaca 1380
acatagatcc ttacatatac acaccctttg gaagtggacc cagaaactgc attggcatga 1440
ggtttgctct catgaacatg aaacttgctc taatcagagt ccttcagaac ttctccttca 1500
aaccttgtaa agaaacacag atccccctga aattaagctt aggaggactt cttcaaccag 1560
aaaaacccgt tgttctaaag gttgagtcaa gggatggcac cgtaagtgga gcctgaattt 1620
tcctaaggac ttctgctttg ctcttcaaga aatctgtgcc tgagaacacc agagacctca 1680
aattactttg tgaatagaac tctgaaatga agatgggctt catccaatgg actgcataaa 1740
taaccgggga ttctgtacat gcattgagct ctctcattgt ctgtgtagag tgttatactt 1800
gggaatataa aggaggtgac caaatcagtg tgaggaggta gatttggctc ctctgcttct 1860
cacgggacta tttccaccac ccccagttag caccattaac tcctcctgag ctctgataag 1920
agaatcaaca tttctcaata atttcctcca caaattatta atgaaaataa gaattatttt 1980
gatggctcta acaatgacat ttatatcaca tgttttctct ggagtattct ataagtttta 2040
tgttaaatca ataaagacca ctttacaaaa gtattatcag atgctttcct gcacattaag 2100
gagaaatcta tagaactgaa tgagaaccaa caagtaaata tttttggtca ttgtaatcac 2160
tgttggcgtg gggcctttgt cagaactaga atttgattat taacataggt gaaagttaat 2220
ccactgtgac tttgcccatt gtttagaaag aatattcata gtttaattat gcctttttg 2280
atcaggcaca gtggctcacg cctgtaatcc tagcagtttg ggaggctgag ccgggtggat 2340
cgcctgaggt caggagttca agacaagcct ggcctacatg gttgaaaccc catctctact 2400
aaaaatacac aaattagcta ggcatggtgg actcgcctgt aatctcacta cacaggaggc 2460
tgaggcagga gaatcacttg aacctgggag gcggatgttg aagtgagctg agattgcacc 2520
actgcactcc agtctgggtg agagtgagac tcagtcttaa aaaaatatgc ctttttgaag 2580
cacgtacatt ttgtaacaaa gaactgaagc tcttattata ttattagttt tgatttaatg 2640
ttttcagccc atctcctttc atatttctgg gagacagaaa acatgtttcc ctacacctct 2700
tgcattccat cctcaacacc caactgtctc gatgcaatga acacttaata aaaaacagtc 2760
gattggtc 2768

<210> 364
<211> 2984
<212> DNA
<213> Homo sapiens

<400> 364
gaggaggaac agaaaagaaa agaaaagaaa aagtgggaaa caaataatct aagaatgagg 60
agaaagcaag aagagtgacc cccttgtggg cactccattg gttttatggc gcctctactt 120
tctggagttt gtgtaaaaca aaaatattat ggtctttgtg cacatttaca tcaagctcag 180
cctgggcggc acagccagat gcgagatgcg tctctgctga tctgagtctg cctgcagcat 240
ggacctgggt cttccctgaa gcatctccag ggctggaggg acgactgcca tgcaccgagg 300

gctcatccat ccacagagca gggcagtggg aggagacgcc atgaccccca tcctcacggt 360
cctgatctgt ctcgggctga gtctgggccc ccggacccac gtgcaggcag ggcacctccc 420
caagcccacc ctctgggctg aaccaggctc tgtgatcacc caggggagtc ctgtgaccct 480
caggtgtcag gggggccagg agacccagga gtaccgtcta tatagagaaa agaaaacagc 540
accctggatt acacggatcc cacaggagct tgtgaagaag ggccagttcc ccatcccatc 600
catcacctgg gaacatgcag ggcggtatcg ctgttactat ggtagcgaca ctgcaggccg 660
ctcagagagc agtgacccccc tggagctggt ggtgacagga gcctacatca aaccccaccct 720
ctcagcccag cccagccccg tggtgaactc aggagggaat gtaaccctcc agtgtgactc 780
acaggtggca tttgatggct tcattctgtg taaggaagga gaagatgaac acccacaatg 840
cctgaactcc cagccccatg cccgtgggtc gtcccgcgcc atcttctccg tgggccccgt 900
gagcccgagt cgcaggtggt ggtacaggtg ctatgcttat gactcgaact ctccctatga 960
gtggtctcta cccagtgatc tcctggagct cctggtccta ggtgtttcta agaagccatc 1020
actctcagtg cagccaggtc ctatcgtggc ccctgaggag accctgactc tgcagtgtgg 1080
ctctgatgct ggctacaaca gatttgttct gtataaggac ggggaacgtg acttccttca 1140
gctcgctggc gcacagcccc aggctgggct ctcccaggcc aacttcaccc tgggccctgt 1200
gagccgctcc tacgggggcc agtacagatg ctacggtgca cacaacctct cctccgagtg 1260
gtcggccccc agcgaccccc tggacatcct gatcgcagga cagttctatg acagagtctc 1320
cctctcggtg cagccgggcc ccacggtggc ctcaggagag aacgtgaccc tgctgtgtca 1380
gtcacaggga tggatgcaaa ctttccttct gaccaaggag gggcagctg atgacccatg 1440
gcgtctaaga tcaacgtacc aatctcaaaa ataccaggct gaattcccca tgggtcctgt 1500
gacctcagcc catgcgggga cctacaggtg ctacggctca cagagctcca aaccctacct 1560
gctgactcac cccagtgacc ccctggagct cgtggtctca ggaccgtctg gggccccag 1620
ctccccgaca acaggcccca cctccacatc tggccctgag gaccagcccc tcaccccccac 1680
cgggtcggat ccccagagtg gtctgggaag gcacctgggg gttgtgatcg gcatcttggt 1740
ggccgtcatc ctactgctcc tcctcctcct cctcctcttc ctcatcctcc gacatcgacg 1800
tcagggcaaa cactggacat cgacccagag aaaggctgat ttccaacatc ctgcaggggc 1860
tgtggggcca gagcccacag acagaggcct gcagtggagg tccagcccag ctgccgatgc 1920
ccaggaagaa aacctctatg ctgccgtgaa gcacacacag cctgaggatg ggtggagat 1980
ggacactcgg agcccacacg atgaagaccc ccaggcagtg acgtatgccg aggtgaaaca 2040
ctccagacct aggagagaaa tggcctctcc tccttcccca ctgtctgggg aattcctgga 2100
cacaaaggac agacaggcgg aagaggacag gcagatggac actgaggctg ctgcatctga 2160
agccccccag gatgtgacct acgcccagct gcacagcttg acccttagac ggaaggcaac 2220
tgagcctcct ccatcccagg aagggccctc tccagctgtg cccagcatct acgccactct 2280
ggccatccac tagcccaggg ggggacgcag accccacact ccatggagtc tggaatgcat 2340
gggagctgcc cccccagtgg acaccattgg accccaccca gcctggatct accccaggag 2400
actctgggaa cttttagggg tcactcaatt ctgcagtata aataactaat gtctctacaa 2460
ttttgaaata aagcaacaga cttctcaata atcaatgaag tagctgagaa aactaagtca 2520
gaaagtgcat taaactgaat cacaatgtaa atattacaca tcaagcgatg aaactggaaa 2580
actacaagcc acgaatgaat gaattaggaa agaaaaaaag taggaaatga atgatcttgg 2640
ctttcctata agaaatttag ggcagggcac ggtggctcac gcctgtaatt ccagcacttt 2700
gggaggccga ggcgggcaga tcacgagttc aggagatcga gaccatcttg gccaacatgg 2760
tgaaaccctg tctctcctaa aaatacaaaa attagctgga tgtggtggca gtgcctgtaa 2820
tcccagctat ttgggaggct gaggcaggag aatcgcttga accagggagt cagaggtttc 2880
agtgagccaa gatcgcacca ctgctctcca gcctggcgac agagggagac tccatctcaa 2940
attaaaaaaa aaaaaaaaaa agaaagaaaa aaaaaaaaaa aaaa 2984

<210> 365
<211> 3061
<212> DNA
<213> Homo sapiens

<400> 365
cggcacgagg cgactttggt ggaggtagtt ctttggcagc gggcatggcg ggtaccgtgg 60
tgctggacga tgtggagctg cgggaggctc agagagatta cctggacttc ctggacgacg 120
aggaagacca gggaatttat cagagcaaag ttcgggagct gatcagtgac aaccaatacc 180
ggctgattgt caatgtgaat gacctgcgca ggaaaaacga gaagagggct aaccggcttc 240
tgaacaatgc ctttgaggag ctggttgcct tccagcgggc cttaaaggat tttgtggcct 300
ccattgatgc tacctatgcc aagcagtatg aggagttcta cgtaggactg gaaggcagct 360
ttggctccaa gcacgtctcc ccgcggactc ttacctcctg cttcctcagc tgtgtggtct 420
gtgtggaggg cattgtcact aaatgttctc tagttcgtcc caaagtcgtc cgcagtgtcc 480
actactgtcc tgctactaag aagaccatag agcgacgtta ttctgatctc accaccctgg 540
tggcctttcc ctccagctct gtctatccta ccaaggatga ggagaacaat ccccttgaga 600
cagaatatgg cctttctgtc tacaaggatc accagaccat caccatccag gagatgccgg 660
agaaggcccc agccggccag ctcccccgct ctgtggacgt cattctggat gatgacttgg 720
tggataaagc gaagcctggt gaccgggttc aggtggtggg aacctaccgt tgccttcctg 780
gaaagaaggg aggctacacc tctgggacct tcaggactgt cctgattgcc tgtaatgtta 840
agcagatgag caaggatgct cagccctctt tctctgctga ggatatagcc aagatcaaga 900
agttcagtaa aacccgatcc aaggatatct ttgaccagct ggccaagtca ttggccccaa 960

gtatccatgg gcatgactat gtcaagaaag caatcctctg cttgctcttg ggaggggtgg 1020
aacgagacct agaaaatggc agccacatcc gtggggacat caatattctt ctaataggag 1080
acccatccgt tgccaagtct cagcttctgc ggtatgtgct ttgcactgca ccccgagcta 1140
tccccaccac tggccggggc tcctctggag tgggtctgac ggctgctgtc accacagacc 1200
aggaaacagg agagcgccgt ctggaagcag gggccatggt cctggctgac cgaggcgtgg 1260
tttgcattga tgaatttgac aaaatgtctg acatggatcg cacagccatc catgaagtga 1320
tggagcaggg tcgagtgacc attgccaagg ctggcatcca tgctcggctg aatgcccgct 1380
gcagtgtttt ggcagctgcc aaccctgtct acggcaggta tgaccagtat aagactccaa 1440
tggagaacat tgggctacag gactcactgc tgtcacgatt tgacttgctc ttcatcatgc 1500
tggatcagat ggatcctgag caggatcggg agatctcaga ccatgtcctt cggatgcacc 1560
gttacagagc acctggggag caggatggcg atgctatgcc cttgggtagt gctgtggata 1620
tcctggccac agatgatccc aactttagcc aggaagatca gcaggacacc cagatttatg 1680
agaagcatga caaccttcta catgggacca agaagaaaaa ggagaagatg gtgagtgcag 1740
cattcatgaa gaagtacatc catgtggcca aaatcatcaa gcctgtcctg acacaggagt 1800
cggccaccta cattgcagaa gagtattcac gcctgcgcag ccaggatagc atgagctcag 1860
acaccgccag gacatctcca gttacagccc gaacactgga aactctgatt cgactggcca 1920
cagcccatgc gaaggcccgc atgagcaaga ctgtggacct gcaggatgca gaggaagctg 1980
tggagttggt ccagtatgct tactttaaga aggttctgga gaaggagaag aaacgtaaga 2040
agcgaagtga ggatgaatca gagacagaag atgaagagga gaaaagccaa gaggaccagg 2100
agcagaagag gaagagaagg aagactcgcc agccagatgc caaagatggg gattcatacg 2160
acccctatga cttcagtgac acagaggagg aaatgcctca agtacacact ccaaagacgg 2220
cagactcaca ggagaccaag gaatcccaga aagtggagtt gagtgaatcc aggttgaagg 2280
cattcaaggt ggccctcttg gatgtgttcc gggaagctca tgcgcagtca atcggcatga 2340
atcgcctcac agaatccatc aaccgggaca gcgaagagcc cttctcttca gttgagatcc 2400
aggctgctct gagcaagatg caggatgaca atcaggtcat ggtgtctgag ggcatcatct 2460
tcctcatctg aggaggcctc gtctctgaac ttgggttgtg ccgagagagt ttgttctgtg 2520
tttcccaccc tctccctgac ccaagtcttt gcctctactc ccttaacagt gttgaattca 2580
actgaaggcg aggaatgttg gtgatgaagc tgagttcagg actcggtgga ccctttggga 2640
atgggtcatg aaagctgcca tggggtgagg aaagaggaga cagtgggaga ggacaatgac 2700
tattgcatct tcattgcaaa agcactggct catccgccct acttcccatc ccacacaaac 2760
ccaattgtaa ataacatatg acttctgagt acttttgggg gcacaactgt ttctgtttg 2820
ctgtttttt gttttgtttt ttttctccag agcactttgg tctagactag gctttgggtg 2880
gttccaattg gtggagagaa gctctgaggc acgtcatgca ggtcaagaaa gctttctttg 2940
cagtagcacc agttaaggtg aatatgtatt gtatcacaaa acaaacccaa tatccagatg 3000
aatatccgag atgttgaata aacttagcca tttcgtacaa aaaaaggggg gcccggtaaa 3060
c 3061

<210> 366
<211> 1360
<212> DNA
<213> Homo sapiens

<400> 366
cggggggttgc tccgtccgtg ctccgcctcg ccatgacttc ctacagctat cgccagtcgt 60
cggccacgtc gtccttcgga ggcctgggcg gcggctccgt gcgttttggg ccgggggtcg 120
cttttcgcgc gcccagcatt cacgggggct ccggcggccg cggcgtatcc gtgtcctccg 180
cccgctttgt gtcctcgtcc tcctcggggg gctacggcgg cggctacggc ggcgtcctga 240
ccgcgtccga cgggctgctg gcgggcaacg agaagctaac catgcagaac ctcaacgacc 300
gcctggcctc ctacctggac aaggtgcgcg ccctggaggc ggccaacggc gagctagagg 360
tgaagatccg cgactggtac cagaagcagg ggcctgggcc ctcccgcgac tacagccact 420
actacacgac catccaggac ctgcgggaca agattcttgg tgccaccatt gagaactcca 480
ggattgtcct gcagatcgac aacgcccgtc tggctgcaga tgacttccga accaagtttg 540
agacggaaca ggctctgcgc atgagcgtgg aggccgacat caacggcctg cgcagggtgc 600
tggatgagct gaccctggcc aggaccgacc tggagatgca gatcgaaggc ctgaaggaag 660
agctggccta cctgaagaag aaccatgagg aggaaatcag tacgctgagg ggccaagtgg 720
gaggccaggt cagtgtggag gtggattccg ctcccggcac cgatctcgcc aagatcctga 780
gtgacatgcg aagccaatat gaggtcatgg ccgagcagaa ccggaaggat gctgaagcct 840
ggttcaccag ccggactgaa gaattgaacc gggaggtcgc tggccacacg gagcagctcc 900
agatgagcag gtccgaggtt actgacctgc ggcgcacccct tcagggtctt gagattgagc 960
tgcagtcaca gctgagcatg aaagctgcct tggaagacac actggcagaa acggaggcgc 1020
gctttggagc ccagctggcg catatccagg cgctgatcag cggtattgaa gcccagctgg 1080
cggatgtgcg agctgatagt gagcggcaga atcaggagta ccagcggctc atggacatca 1140
agtcgcggct ggagcaggag attgccacct accgcagcct gctcgaggga caggaagatc 1200
actacaacaa tttgtctgcc tccaaggtcc tctgaggcag caggctctgg ggcttctgct 1260
gtcctttgga gggtgtcttc tgggtagagg gatgggaagg aagggaccct tacccccggc 1320
tcttctcctg acctgccaat aaaaatttat ggtccaaggg 1360

<210> 367

<211> 1412
<212> DNA
<213> Homo sapiens

<400> 367
cggggtcgtc cgcaaagcct gagtcctgtc ctttctctct ccccggacag catgagcttc 60
accactcgct ccaccttctc caccaactac cggtccctgg gctctgtcca ggcgcccagc 120
tacggcgccc ggccggtcag cagcgcggcc agcgtctatg caggcgctgg gggctctggt 180
tcccggatct ccgtgtcccg ctccaccagc ttcaggggcg gcatggggtc cgggggcctg 240
gccaccggga tagccggggg tctggcagga atgggaggca tccagaacga gaaggagacc 300
atgcaaagcc tgaacgaccg cctggcctct tacctggaca gagtgaggag cctggagacc 360
gagaaccgga ggctggagag caaaatccgg gagcacttgg agaagaaggg accccaggtc 420
agagactgga gccattactt caagatcatc gaggacctga gggctcagat cttcgcaaat 480
actgtggaca atgcccgcat cgttctgcag attgacaatg cccgtcttgc tgctgatgac 540
tttagagtca agtatgagac agagctggcc atgcgccagt ctgtggagaa cgacatccat 600
gggctccgca aggtcattga tgacaccaat atcacacgac tgcagctgga gacagagatc 660
gaggctctca aggaggagct gctcttcatg aagaagaacc acgaagagga agtaaaaggc 720
ctacaagccc agattgccag ctctgggttg accgtggagg tagatgcccc caaatctcag 780
gacctcgcca agatcatggc agacatccgg gcccaatatg acgagctggc tcggaagaac 840
cgagaggagc tagacaagta ctggtctcag cagattgagg agagcaccac agtggtcacc 900
acacagtctg ctgaggttgg agctgctgag acgacgctca cagagctgag acgtacagtc 960
cagtccttgg agatcgacct ggactccatg agaaatctga aggccagctt ggagaacagc 1020
ctgagggagg tggaggcccg ctacgcccta cagatggagc agctcaacgg gatcctgctg 1080
caccttgagt cagagctggc acagacccgg gcagagggac agcgccaggc ccaggagtat 1140
gaggccctgc tgaacatcaa ggtcaagctg gaggctgaga tcgccaccta ccgccgcctg 1200
ctggaagatg gcgaggactt taatcttggt gatgccttgg acagcagcaa ctccatgcaa 1260
accatccaaa agaccaccac ccgccggata gtggatggca aagtggtgtc tgagaccaat 1320
gacaccaaag ttctgaggca ttaagccagc agaagcaggg taccctttgg ggagcaggag 1380
gccaataaaa agttcagagt tcattggatg tc 1412

<210> 368
<211> 1075
<212> DNA
<213> Homo sapiens

<400> 368
cgcagcaaac acatccgtag aaggcagcgc ggccgccgag agccgcagcg ccgctcgccc 60
gccgcccccc accccgccgc cccgcccggc gaattgcgcc ccgcgcccct cccctcgcgc 120
ccccgagaca aagaggagag aaagtttgcg cggccgagcg gggcaggtga ggagggtgag 180
ccgcgcggga ggggcccgcc tcggccccgg ctcagccccc gcccgcgccc ccagcccgcc 240
gccgcgagca gcgcccggac cccccagcgg cggcccccgc ccgcccagcc ccccggcccg 300
ccatgggcgc cgcggcccgc accctgcggc tggcgctcgg cctcctgctg ctggcgacgc 360
tgcttcgccc ggccgacgcc tgcagctgct ccccggtgca cccgcaacag gcgttttgca 420
atgcagatgt agtgatcagg gccaaagcgg tcagtgagaa ggaagtggac tctggaaacg 480
acatttatgg caaccctatc aagaggatcc agtatgagat caagcagata aagatgttca 540
aagggcctga gaaggatata gagtttatct acacggcccc ctcctcggca gtgtgtgggg 600
tctcgctgga cgttggagga aagaaggaat atctcattgc aggaaaggcc gagggggacg 660
gcaagatgca catcaccctc tgtgacttca tcgtgccctg ggacaccctg agcaccaccc 720
agaagaagag cctgaaccac aggtaccaga tgggctgcga gtgcaagatc acgcgctgcc 780
ccatgatccc gtgctacatc tcctccccgg acgagtgcct ctggatggac tgggtcacag 840
agaagaacat caacgggcac caggccaagt tcttcgcctg catcaagaga agtgacggct 900
cctgtgcgtg gtaccgcggc gcggcgcccc ccaagcagga gtttctcgac atcgaggacc 960
cataagcagg cctccaacgc ccctgtggcc aactgcaaaa aaagcctcca agggtttcga 1020
ctggtccagc tctgacatcc cttcctggaa acagcatgaa taaaacactc atccc 1075

<210> 369
<211> 1127
<212> DNA
<213> Homo sapiens

<400> 369
cacgggcggg gcggggcctg ggtccaccgg ggttctgagg ggagactgag gtcctgagcc 60
gacagcctca gctccctgcc aggccagacc cggcagacag atgagggccc aggaggcctg 120
gcgggcctgg gggcgctacg gtgggagagg aagccagggg tacctgcctc tgccttccag 180
ggccaccgtt ggccccagct gtgccttgac tacgtaacat cttgtcctca cagcccagag 240
catgttccag atcccagagt ttgagccgag tgagcaggaa gactccagct ctgcagagag 300
gggcctgggc cccagccccg caggggacgg gccctcaggc tccggcaagc atcatcgcca 360
ggccccaggc ctcctgtggg acgccagtca ccagcaggag cagccaacca gcagcagcca 420

tcatggaggc gctggggctg tggagatccg gagtcgccac agctcctacc ccgcggggac 480
ggaggacgac gaagggatgg gggaggagcc cagccccttt cggggccgct cgcgctcggc 540
gcccccccaac ctctgggcag cacagcgcta tggccgcgag ctccggagga tgagtgacga 600
gtttgtggac tcctttaaga agggacttcc tcgcccgaag agcgcgggca cagcaacgca 660
gatgcggcaa agctccagct ggacgcgagt cttccagtcc tggtgggatc ggaacttggg 720
caggggaagc tccgcccct cccagtgacc ttcgctccac atcccgaaac tccacccgtt 780
cccactgccc tgggcagcca tcttgaatat gggcggaagt acttccctca ggcctatgca 840
aaaagaggat ccgtgctgtc tcctttggag ggagggctga cccagattcc cttccggtgc 900
gtgtgaagcc acggaaggct tggtcccatc ggaagttttg ggttttccgc ccacagccgc 960
cggaagtggc tccgtggccc cgccctcagg ctccgggctt tcccccaggc gcctgcgcta 1020
agtcgcgagc caggtttaac cgttgcgtca ccgggacccg agcccccgcg atgccctggg 1080
ggccgtgctc actaccaaat gttaataaag cccgcgtctg tgccgcc 1127

<210> 370
<211> 1890
<212> DNA
<213> Homo sapiens

<400> 370
cttaataaga agagaaggct tcaatggaac cttttgtggt cctggtgctg tgtctctctt 60
ttatgcttct cttttcactc tggagacaga gctgtaggag aaggaagctc cctcctggcc 120
ccactcctct tcctattatt ggaaatatgc tacagataga tgttaaggac atctgcaaat 180
ctttcaccaa tttctcaaaa gtctatggtc ctgtgttcac cgtgtatttt ggcatgaatc 240
ccatagtggt gtttcatgga tatgaggcag tgaaggaagc cctgattgat aatggagagg 300
agtttttctgg aagaggcaat tccccaatat ctcaaagaat tactaaagga cttggaatca 360
tttccagcaa tggaaagaga tggaaggaga tccggcgttt ctccctcaca aacttgcgga 420
attttgggat ggggaagagg agcattgagg accgtgttca agaggaagct cactgccttg 480
tggaggagtt gagaaaaacc aaggcttcac cctgtgatcc cactttcatc ctgggctgtg 540
ctccctgcaa tgtgatctgc tccgttgttt tccagaaacg atttgattat aaagatcaga 600
atttctcac cctgatgaaa agattcaatg aaaacttcag gattctgaac tccccatgga 660
tccaggtctg caataatttc cctctactca ttgattgttt cccaggaact cacaacaaag 720
tgcttaaaaa tgttgctctt acacgaagtt acattaggga gaaagtaaaa gaacaccaag 780
catcactgga tgttaacaat cctcgggact ttatggattg cttcctgatc aaaatggagc 840
aggaaaagga caaccaaaag tcagaattca atattgaaaa cttggttggc actgtagctg 900
atctatttgt tgctggaaca gagacaacaa gcaccactct gagatatgga ctcctgctcc 960
tgctgaagca cccagaggtc acagctaaag tccaggaaga gattgatcat gtaattggca 1020
gacacaggag cccctgcatg caggatagga gccacatgcc ttacactgat gctgtagtgc 1080
acgagatcca gagatacagt gaccttgtcc ccaccggtgt gccccatgca gtgaccactg 1140
atactaagtt cagaaactac ctcatcccca agagctttga taacaagata atgctggctg 1200
cataaaacta gggcacaacc ataatggcat tactgacttc cgtgctacat gatgacaaag 1260
aatttcctaa tccaaatatc tttgaccctg gccactttct agataagaat ggcaacttta 1320
agaaaagtga ctacttcatg cctttctcag caggaaaacg aatttgtgca ggagaaggac 1380
ttgcccgcat ggagctattt ttatttctaa ccacaatttt acagaacttt aacctgaaat 1440
ctgttgatga tttaaagaac ctcaatacta ctgcagttac caaagggatt gtttctctgc 1500
caccctcata ccagatctgc ttcatccctg tctgaagaat gctagcccat ctggctgctg 1560
atctgctatc acctgcaact cttttttat caaggacatt cccactatta tgtcttctct 1620
gacctctcat caaatcttcc cattcactca atatcccata agcatccaaa ctccattaag 1680
gagagttgtt caggtcactg cacaaatata tctgcaatta ttcatactct gtaacacttg 1740
tattaattgc tgcatatgct aatacttttc taatgctgac tttttaatat gttatcactg 1800
taaaacacag aaaagtgatt aatgaatgat aatttagtcc atttcttttg tgaatgtgct 1860
aaataaaaag tgttattaat tgctggttca 1890

<210> 371
<211> 4946
<212> DNA
<213> Homo sapiens

<400> 371
agtcagccct gctgccagcc agtgccgggt gctggggact cagggaggcc cgccgggacc 60
actgcgggac agtgagccga gcagaagctg gaacgcagga gaggaaggag agggggcggt 120
cagggctctc aggagccggg tcctgggcaa ggcgcagccg ttttcaaatt ttcaggaaag 180
cggtcggctc acactcgagc agtaaaaaga tgcctctggg gaggaggccc gtgcagctct 240
ccgggcaatg gtggtggctc ggcctagaga ggcggtagtg gaacgcagac cctggtgggg 300
gaatgacatc aagggaggag acgggcggga ccccagattt ctgcctgtgg gcgatggaag 360
tgaggttcac tggccagcgg agccggacac agaacgcgca aaacgccgtg taggcctgga 420
ggagccgaag agcaggcgga ccccctccgc gggggaacag tttccgccgg gagcacaaag 480
caacggaccg gaagtggggg gcggaagtgc agtgggctca gcgccgactg cgcgcctctg 540
cccgcgaaaa ctctgagctg gctgacagct ggggacgggt ggcggccctc gactggagtc 600

```
ggttgagttc ctgagggacc ccggttctgg aaggttcgcc gcggagacaa gtgagcagtc 660
tgtgccatag ggattctcga agagaacagc gttgtgtccc agtgcacatg ctcgcatcgc 720
ttaccaggag tgcccgagac cctaagatgt tcggagtggt tttttcgcac agacccgaat 780
agcctgcccc tcagccacgc tctgtgccct tctgagaaca ggctgatatg cccaagatag 840
tcctgaatgg tgtgaccgta gacttccctt tccagcccta caaatgccaa caggagtaca 900
tgaccaaggt cctggaatgt ctgcagcaga aggtgaatgg catcctggag agccctacgg 960
gtacagggaa gacgctgtgc ctgctgtgca ccacgctggc ctggcgagaa cacctccgag 1020
acggcatctc tgcccgcaag attgccgaga gggcgcaagg agagcttttc ccggatcggg 1080
ccttgtcatc ctggggcaac gctgctgctg ctgctggaga ccccatagct tgctacacgg 1140
acatcccaaa gattatttac gcctccagga cccactcgca actcacacag gtcatcaacg 1200
agcttcggaa cacctcctac cggcctaagg tgtgtgtgct gggctcccgg gagcagctgt 1260
gcatccatcc tgaggtgaag aaacaagaga gtaaccatct acagatccac ttgtgccgta 1320
agaaggtggc aagtcgctcc tgtcatttct acaacaacgt agaagaaaaa agcctggagc 1380
aggagctggc cagccccatc ctggacattg aggacttggt caagagcgga agcaagcaca 1440
gggtgtgccc ttactacctg tcccggaacc tgaagcagca agccgacatc atattcatgc 1500
cgtacaatta cttgttggat gccaagagcc gcagagcaca caacattgac ctgaagggga 1560
cagtcgtgat ctttgacgaa gctcacaacg tggagaagat gtgtgaagaa tcggcatcct 1620
ttgacctgac tccccatgac ctggcttcag gactggacgt catagaccag gtgctggagg 1680
agcagaccaa ggcagcgcag cagggtgagc cccacccgga gttcagcgcg gactccccca 1740
gcccagggct gaacatggag ctggaagaca ttgcaaagct gaagatgatc ctgctgcgcc 1800
tggagggggc catcgatgct gttgagctgc ctggagacga cagcggtgtc accaagccag 1860
ggagctacat ctttgagctg tttgctgaag cccagatcac gtttcagacc aagggctgca 1920
tcctggactc gctggaccag atcatccagc acctggcagg acgtgctgga gtgttcacca 1980
acacggccgg actgcagaag ctggcggaca ttatccagat tgtgttcagt gtggacccct 2040
ccgagggcag ccctggttcc ccagcagggc tgggggcctt acagtcctat aaggtgcaca 2100
tccatcctga tgctggtcac cggaggacgg ctcagcggtc tgatgcctgg agcaccactg 2160
cagccagaaa gcgagggaag gtgctgagct actggtgctt cagtcccggc cacagcatgc 2220
acgagctggt ccgccagggc gtccgctccc tcatccttac cagcggcacg ctggccccgg 2280
tgtcctcctt tgctctggag atgcagatcc ctttcccagt ctgcctggag aacccacaca 2340
tcatcgacaa gcaccagatc tgggtggggg tcgtccccag aggccccgat ggagcccagt 2400
tgagctccgc gtttgacaga cggttttccg aggagtgctt atcctccctg ggaaggctc 2460
tgggcaacat cgcccgcgtg gtgccctatg ggctcctgat cttcttccct tcctatcctg 2520
tcatggagaa gagcctggag ttctggcggg cccgcgactt ggccaggaag atggaggcgc 2580
tgaagccgct gtttgtggag cccaggagca aaggcagctt ctccgagacc atcagtgctt 2640
actatgcaag ggttgccgcc cctgggtcca ccggcgccac cttcctggcg gtctgccggg 2700
gcaaggccag cgaggggctg gacttctcag acacgaatgg ccgtggtgtg attgtcacgg 2760
gcctcccgta cccccccacgc atggaccccc gggttgtcct caagatgcag ttcctggatg 2820
agatgaaggg ccagggtggg gctgggggcc agttcctctc tgggcaggag tggtaccggc 2880
agcaggcgtc cagggctgtg aaccaggcca tcgggcgagt gatccggcac cgccaggact 2940
acggagctgt cttcctctgt gaccacaggt tcgcctttgc cgacgcaaga gcccaactgc 3000
cctcctgggt gcgtccccac gtcagggtgt atgacaactt tggccatgtc atccgagacg 3060
tggcccagtt cttccgtgtt gccgagcgaa ctatgccagc gccggccccc cgggctacag 3120
cacccagtgt gcgtggagaa gatgctgtca gcgaggccaa gtcgcctggc cccttcttct 3180
ccaccaggaa agctaagagt ctggacctgc atgtccccag cctgaagcag aggtcctcag 3240
ggtcaccagc tgccggggac cccgagagta gcctgtgtgt ggagtatgag caggagccag 3300
ttcctgcccg gcagaggccc agggggctgc tggccgccct ggagcacagc gaacagcggg 3360
cggggagccc tggcgaggag caggcccaca gctgctccac cctgtccctc ctgtctgaga 3420
agaggccggc agaagaaccg cgaggaggga ggaagaagat ccggctggtc agccacccgg 3480
aggagcccgt ggctggtgca cagacggaca gggccaagct cttcatggtg gccgtgaagc 3540
aggagttgag ccaagccaac tttgccacct tcacccaggc cctgcaggac tacaagggtt 3600
ccgatgactt cgccgccctg gccgcctgtc tcggccccct ctttgctgag gaccccaaga 3660
agcacaacct gctccaaggc ttctaccagt ttgtgcggcc ccaccataag cagcagtttg 3720
aggaggtctg tatccagctg acaggacgag gctgtggcta tcggcctgag cacagcattc 3780
cccgaaggca gcgggcacag ccggtcctgg accccactgg aagaacggcg ccggatccca 3840
agctgaccgt gtccacggct gcagcccagc agctggaccc ccaagagcac ctgaaccagg 3900
gcaggcccca cctgtcgccc aggccacccc caacaggaga ccctggcagc caaccacagt 3960
gggggtctgg agtgcccaga gcagggaagc agggccagca cgccgtgagc gcctacctgg 4020
ctgatgcccg cagggccctg gggtccgcgg gctgtagcca actcttggca gcgctgacag 4080
cctataagca agacgacgac ctcgacaagg tgctggctgt gttggccgcc ctgaccactg 4140
caaagccaga ggacttcccc ctgctgcaca ggttcagcat gtttgtgcgt ccacaccaca 4200
agcagcgctt ctcacagacg tgcacagacc tgaccggccg gccctacccg ggcatggagc 4260
caccgggacc ccaggaggag aggcttgccg tgcctcctgt gcttacccac agggctcccc 4320
aaccaggccc ctcacggtcc gagaagaccg ggaagaccca gagcaagatc tcgtccttcc 4380
ttagacagag gccagcaggg actgtggggg cgggcggtga ggatgcaggt cccagccagt 4440
cctcaggacc tccccacggg cctgcagcat ctgagtgggg cctctaggat gtgcccagcc 4500
tgccacaccg cctccaggaa gcagagcgtc atgcaggtct tctggccaga gccccagtga 4560
gtgcccacgg aggcccccag cacacccaac gtggcttgat cacctgcctg tccagctctg 4620
gtgggccaag aacccaccca acagaatagg ccagcccatg ccagccggct tggcccgctg 4680
```

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/07713

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; G01N 33/53
US CL : 435/6, 7.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y --- A	US 6,316,208 B1 (ROBERTS et al.) 13 November 2001 (13.11.2001), columns 18-20 and 43-47.	18-24,32,37,38 --- 1-17,25-31,33-36,39-45
A	US 6,180,333 B1 (GIORDANO) 30 January 2001 (30.01.2001).	1-45
A	US 5,563,035 A (WEIGEL) 08 October 1996 (08.10.1996).	1-45

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 June 2003 (10.06.2003)	03 JUL 2003
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Felicia D. Roberts for Kenneth R Horlick Telephone No. 703-308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/07713

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-17, drawn to a method for predicting clinical outcome for a patient diagnosed with cancer.

Group II, claim(s) 18-24, drawn to a method of predicting the likelihood of the recurrence of cancer following treatment in a cancer patient.

Group III, claim(s) 25-31, drawn to a method for classifying cancer.

Group IV, claim(s) 32-40, drawn to a method for predicting the likelihood of long-term survival of a breast cancer patient, and an array for use therein.

Group V, claim(s) 41 and 44, drawn to a method of predicting the likelihood of long-term survival of a patient diagnosed with invasive breast cancer, and an array for use therein.

Group VI, claim(s) 42, 43, and 45, drawn to a method of predicting the likelihood of long-term survival of a patient diagnosed with estrogen receptor-positive invasive breast cancer, and an array for use therein.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: each of the groups corresponds to a specific relationship between a specific type of cancer and a specific set of genes; thus, there is clearly no special technical feature in common.

Continuation of B. FIELDS SEARCHED Item 3:
USPAT, PGPUB, DERWENT, MEDLINE, BIOSIS
search terms: cancer, tumor, prognosis, expression, p27, p53BP2, etc.